

=> d his

(FILE 'HOME' ENTERED AT 14:19:58 ON 23 AUG 2005)
SET COST OFF

FILE 'HCAPLUS' ENTERED AT 14:20:07 ON 23 AUG 2005

L1 1 S US20040209802/PN OR (US2003-706701# OR EP2002-26342)/AP,PRN
E LEHMAN P/AU
L2 52 S E3-E7,E9-E12
E LEHMANN P/AU
L3 267 S E3-E6,E11-E14
E OREDDIGER R/AU
E ROEDDIGER R/AU
L4 9 S E3,E4
E ROEDIGER R/AU
L5 2 S E4
E RODIGER R/AU
L6 1 S E4
E RODDIGER R/AU
L7 2 S E4
E WALTER MATSUI/AU
L8 4 S E4,E5
E MATSUI R/AU
L9 15 S E3
E MATSUI W/AU
SEL RN L1

FILE 'REGISTRY' ENTERED AT 14:22:38 ON 23 AUG 2005

L10 7 S E1-E7
L11 6 S L10 AND ERYTHROPOIETIN
L12 1 S L10 NOT L11
E ERYTHROPOIETIN
L13 1792 S E3
L14 1792 S L11,L13
E IRON/CN
L15 1 S E3
E FE/MF
L16 30 S E3 NOT MASS
L17 30 S L15,L16

FILE 'HCAPLUS' ENTERED AT 14:24:56 ON 23 AUG 2005

L18 9810 S L14
L19 11804 S ?ERYTHROPOIETIN?
L20 129 S DARBEPOETIN?(S) (ALPHA OR ALFA)
L21 135 S ?DARBEPOETIN?
L22 6067 S EPO OR EPREX
L23 298 S EPOETIN?(S) (ALFA OR ALPHA)
L24 100 S EPOETIN?(S) BETA
L25 458 S EPOETIN
L26 42 S ARANESP
L27 14463 S L18-L26
L28 655 S L27 AND L17
L29 1236 S L27 AND (FE OR IRON)
L30 1243 S L28,L29
E HEART DISEASE/CT
E E4+ALL
E E2+ALL
L31 86736 S E7+OLD,NT
L32 29 S L30 AND L31
L33 0 S E90+OLD,NT AND L30

L34 47 S E92+OLD,NT AND L30
L35 36 S L32,L34 AND (PY<=2002 OR PRY<=2002 OR AY<=2002)
L36 1 S L32,L34 AND L1-L9
L37 3 S L35 AND ?CONJUGAT?
L38 2 S L37 NOT 3/SC
L39 2 S L36,L38
L40 33 S L35 NOT L36-L39
SEL DN AN 6-9 13-15 19-27
L41 16 S L40 AND E1-E48
L42 18 S L39,L41
L43 597 S ?RHUEPO?
L44 155 S L43 AND (L17 OR FE OR IRON)
L45 3 S L44 AND L31
E HEART, DISEASE/CT
E E3+ALL
L46 5 S L44 AND E92+OLD,NT
L47 5 S L45,L46
L48 4 S L47 NOT 2005/PY
L49 19 S L42,L48 AND L1-L9,L18-L48
L50 14474 S L27,L43
L51 360 S L50 AND ?CONJUGAT?
L52 330 S L50 AND ?GLYCOSYLAT?
L53 194 S L50 AND (PEG OR PEGYLAT?)
L54 55 S L50 AND (POLYOXYETHYLENE OR POLYETHYLENEGLYCOL OR POLYETHYLEN
L55 4 S L50 AND POLY() (OXYETHYLENE OR ETHYLENEGLYCOL OR ETHYLENEOXIDE
L56 24 S L50 AND POLY() (OXY ETHYLENE OR ETHYLENE GLYCOL OR ETHYLENE OX
L57 237 S L50 AND (POLYOXY ETHYLENE OR POLYETHYLENE GLYCOL OR POLYETHYL
L58 316 S L50 AND POLYOXYALKYLENE

FILE 'REGISTRY' ENTERED AT 14:42:28 ON 23 AUG 2005

L59 1 S 25322-68-3
L60 0 S L14 AND C2H4O

FILE 'HCAPLUS' ENTERED AT 14:42:46 ON 23 AUG 2005

L61 266 S L50 AND L59
L62 986 S L51-L58,L61
L63 804 S L62 AND (PY<=2002 OR PRY<=2002 OR AY<=2002)
L64 32 S L63 AND (L17 OR FE OR IRON)
L65 30 S L64 AND L18

FILE 'REGISTRY' ENTERED AT 14:44:41 ON 23 AUG 2005

L66 1 S L14 AND NC4/ES
L67 11 S L14 AND S/ELS

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L68 12350 S L27 AND (PY<=2002 OR PRY<=2002 OR AY<=2002)
L69 1036 S L68 AND (L17 OR FE OR IRON)
L70 1808 S L63-L65,L69
L71 1808 S L70 OR L70
L72 500 S L71 RAN=(2001:686932,)
L73 500 S L71 RAN=(1997:740129,2001:679500)
L74 808 S L71 RAN=(,1997:730870)

FILE 'REGISTRY' ENTERED AT 14:48:11 ON 23 AUG 2005

FILE 'HCAPLUS' ENTERED AT 14:48:17 ON 23 AUG 2005

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L75 SEL L74 1- RN : 3039 TERMS
SET SMARTSELECT OFF

L76 FILE 'REGISTRY' ENTERED AT 14:48:35 ON 23 AUG 2005
3035 S L75

FILE 'HCAPLUS' ENTERED AT 14:48:58 ON 23 AUG 2005
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L77 SEL L73 1- RN : 4980 TERMS
SET SMARTSELECT OFF

L78 FILE 'REGISTRY' ENTERED AT 14:49:13 ON 23 AUG 2005
4980 S L77

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SET SMARTSELECT ON
L79 SEL L72 1- RN : 43982 TERMS
SET SMARTSELECT OFF

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L81 49174 S L76,L78,L80
L82 455 S L81 AND C2H4O
L83 55 S L82 AND NC4/ES
L84 1 S L83 AND S/ELS
L85 54 S L83 NOT L84
L86 STR
L87 50 S L86
L88 STR L86
L89 50 S L88
L90 15844 S L86 FUL
L91 86 S L90 AND C2H4O
L92 28 S L91 AND 1/NR NOT P/ELS
SEL RN 4 6-9 22 28
L93 7 S L92 AND E1-E7
L94 58 S L91 NOT L92
L95 35 S L94 NOT P/ELS

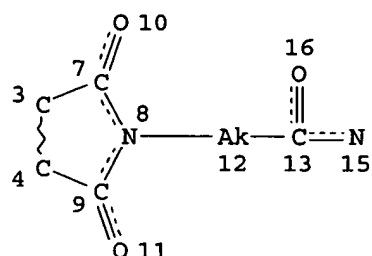
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L96 8 S L93
L97 0 S L96 AND L50
L98 136 S L51,L52 AND L53-L58,L61
L99 110 S L98 AND (PY<=2002 OR PRY<=2002 OR AY<=2002)
L100 18 S L99 AND L51 AND L52
L101 0 S L100 AND L31
L102 6 S L98 AND L31
L103 4 S L99 AND L31
L104 6 S L102,L103
L105 18 S L100 NOT L104
SEL DN AN 3 7 9 12 13 15 16 17
L106 8 S E8-E31 AND L105
SEL DN AN L48 1 4
L107 2 S L48 AND E32-E37
L108 27 S L49,L106,L107
SEL HIT RN

FILE 'REGISTRY' ENTERED AT 15:23:50 ON 23 AUG 2005
L109 19 S E38-E56
L110 15 S L109 AND L14
L111 3 S L109 AND L17
L112 1 S L109 AND L59

=> d sta que 193

L86

STR



NODE ATTRIBUTES:

DEFAULT MLEVEL IS ATOM

DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:

RING(S) ARE ISOLATED OR EMBEDDED

NUMBER OF NODES IS 11

STEREO ATTRIBUTES: NONE

L90 15844 SEA FILE=REGISTRY SSS FUL L86

L91 86 SEA FILE=REGISTRY ABB=ON PLU=ON L90 AND C2H4O

L92 28 SEA FILE=REGISTRY ABB=ON PLU=ON L91 AND 1/NR NOT P/ELS

L93 7 SEA FILE=REGISTRY ABB=ON PLU=ON L92 AND (321936-04-3/BI OR
724722-33-2/BI OR 724722-36-5/BI OR 724722-89-8/BI OR 724722-92-3/BI OR 725273-90-5/BI OR 88504-24-9/BI)

=> fil hcaplus

FILE 'HCAPLUS' ENTERED AT 15:25:04 ON 23 AUG 2005

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FILE COVERS 1907 - 23 Aug 2005 VOL 143 ISS 9

FILE LAST UPDATED: 22 Aug 2005 (20050822/ED)

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This file contains CAS Registry Numbers for easy and accurate substance identification.

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L108 ANSWER 1 OF 27 HCAPLUS COPYRIGHT 2005 ACS on STN

AN 2004:996201 HCAPLUS

DN 141:422003

TI Cell-free oligosaccharide remodeling and glycoPEGylation methods and the

proteins/peptides produced

IN De Frees, Shawn; Zopf, David; Bayer, Robert; Bowe, Caryn; Hakes, David;
Chen, Xi

PA Neose Technologies, Inc., USA

SO PCT Int. Appl., 1024 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 15

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2004099231	A2	20041118	WO 2004-US11494	20040409
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
	RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, BG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	US 2004043446	A1	20040304	US 2003-411037	20030409 <--
	US 2004063911	A1	20040401	US 2003-411026	20030409 <--
	US 2004077836	A1	20040422	US 2003-410962	20030409 <--
	US 2004082026	A1	20040429	US 2003-411049	20030409 <--
	US 2004115168	A1	20040617	US 2003-410930	20030409 <--
	US 2004126838	A1	20040701	US 2003-410997	20030409 <--
	US 2004132640	A1	20040708	US 2003-411012	20030409 <--
	US 2004142856	A1	20040722	US 2003-410913	20030409 <--
	US 2005031584	A1	20050210	US 2003-410980	20030409 <--
	US 2005100982	A1	20050512	US 2003-410897	20030409 <--
PRAI	US 2003-410897	A	20030409		
	US 2003-410913	A	20030409		
	US 2003-410930	A	20030409		
	US 2003-410945	A	20030409		
	US 2003-410962	A	20030409		
	US 2003-410980	A	20030409		
	US 2003-410997	A	20030409		
	US 2003-411012	A	20030409		
	US 2003-411026	A	20030409		
	US 2003-411037	A	20030409		
	US 2003-411043	A	20030409		
	US 2003-411044	A	20030409		
	US 2003-411049	A	20030409		
	US 2001-328523P	P	20011010	<--	
	US 2001-344692P	P	20011019	<--	
	US 2001-334233P	P	20011128	<--	
	US 2001-334301P	P	20011128	<--	
	US 2002-387292P	P	20020607	<--	
	US 2002-391777P	P	20020625	<--	
	US 2002-396594P	P	20020717	<--	
	US 2002-404249P	P	20020816	<--	
	US 2002-407527P	P	20020828	<--	
	WO 2002-US32263	A2	20021009	<--	
	US 2002-287994	A2	20021105	<--	
	US 2003-360770	A2	20030106		
	US 2003-438582P	P	20030106		
	US 2003-360779	A2	20030219		

US 2003-448381P P 20030219

AB The invention includes methods and compns. for remodeling a peptide mol., including the addition or deletion of one or more glycosyl groups to a peptide, and/or the addition of a modifying group to a peptide. In vitro methods for addition and/or deletion of sugars to or from a glypeptide mol. are carried out in a manner as to provide a peptide mol. having a specific customized or desired **glycosylation** pattern, preferably including the addition of a modified sugar. The peptide is enzymically treated in vitro by the systematic addition of the appropriate enzymes and substrates. A key feature of the invention therefore is to take a peptide produced by any cell type and generate a core glycan structure on the peptide, following which the glycan structure is then remodeled in vitro to generate a peptide having a **glycosylation** pattern suitable for therapeutic use in a mammal. The blood-circulation half-life of the selected peptide is extended by **conjugating** the peptide to a synthetic or natural polymer of a size sufficient to retard the filtration of the protein by the glomerulus, as illustrated by **conjugating erythropoietin** to albumin via a **polyethylene glycol (PEG)** linker using a combination of chemical and enzymic modifications.

IT 11096-26-7P, Erythropoietin

RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); PAC (Pharmacological activity); PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(cell-free oligosaccharide remodeling and glycoPEGylation methods and the proteins/peptides produced)

RN 11096-26-7 HCAPLUS

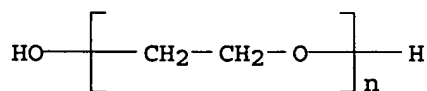
CN Erythropoietin (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

IT 25322-68-3, Poly(ethylene glycol)

RL: BSU (Biological study, unclassified); RCT (Reactant); THU (Therapeutic use); BIOL (Biological study); RACT (Reactant or reagent); USES (Uses)
(cell-free oligosaccharide remodeling and glycoPEGylation methods and the proteins/peptides produced)

RN 25322-68-3 HCAPLUS

CN Poly(oxy-1,2-ethanediyl), α -hydro- ω -hydroxy- (9CI) (CA INDEX NAME)

L108 ANSWER 2 OF 27 HCAPLUS COPYRIGHT 2005 ACS on STN

AN 2004:467755 HCAPLUS

DN 141:34188

TI Methods for the use of **erythropoietin** and its derivatives for the treatment of heart diseasesIN **Lehmann, Paul; Roeddiger, Ralf; Walter-Matsui, Ruth**

PA F. Hoffmann-La Roche A.-G., Switz.

SO PCT Int. Appl., 31 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

PATENT NO.

KIND

DATE

APPLICATION NO.

DATE

PI WO 2004047858 A1 20040610 WO 2003-EP12822 20031117 <--
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE,
GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK,
LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ,
OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM,
TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ,
BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE,
ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK,
TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
US 2004209802 A1 20041021 US 2003-706701 20031112 <--

PRAI EP 2002-26342 A 20021122 <--

AB The present invention relates to the use of **erythropoietin** for
the treatment of disturbances of **iron** distribution in heart
diseases.

IT **702719-61-7, Erythropoietin (human) 702719-62-8**
, Erythropoietin (human)

RL: PAC (Pharmacological activity); PRP (Properties); THU (Therapeutic
use); BIOL (Biological study); USES (Uses)

(amino acid sequence; methods for use of **erythropoietin** (
EPO) and its derivs. for treatment of heart diseases)

RN 702719-61-7 HCAPLUS

CN Erythropoietin (human) (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

RN 702719-62-8 HCAPLUS

CN Erythropoietin (human) (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

IT **7439-89-6, Iron, biological studies**

RL: BSU (Biological study, unclassified); BIOL (Biological study)
(disturbances in cardiac distribution; methods for use of
erythropoietin (EPO) and its derivs. for treatment of
heart diseases)

RN 7439-89-6 HCAPLUS

CN Iron (7CI, 8CI, 9CI) (CA INDEX NAME)

Fe

IT **11096-26-7, Erythropoietin**

RL: PAC (Pharmacological activity); PRP (Properties); THU (Therapeutic
use); BIOL (Biological study); USES (Uses)

(methods for use of **erythropoietin (EPO)** and its
derivs. for treatment of heart diseases)

RN 11096-26-7 HCAPLUS

CN Erythropoietin (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

IT **11096-26-7D, Erythropoietin, conjugates and**
derivs. 113427-24-0, Epoetin alfa

122312-54-3, Epoetin beta 209810-58-2

, Darbepoetin alfa

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
(Biological study); USES (Uses)

(methods for use of **erythropoietin (EPO)** and its
derivs. for treatment of heart diseases)

RN 11096-26-7 HCAPLUS
CN Erythropoietin (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

RN 113427-24-0 HCAPLUS
CN 1-165-Erythropoietin (human clone λ HEPOFL13 protein moiety),
glycoform α (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

RN 122312-54-3 HCAPLUS
CN 1-165-Erythropoietin (human clone λ HEPOFL13 protein moiety),
glycoform β (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

RN 209810-58-2 HCAPLUS
CN Erythropoietin [30-asparagine,32-threonine,87-valine,88-asparagine,90-threonine] (human) (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

RETABLE

Referenced Author (RAU)	Year (RPY)	VOL (RVL)	PG (RPG)	Referenced Work (RWK)	Referenced File
de Valk, B	1999	159	1542	ARCHIVES OF INTERNAL	MEDLINE
Ernst, S	2002			US 2002115833 A1	HCAPLUS
La Roche, H	2003			WO 03025583 A	HCAPLUS
Peeters, H	1999	18	201	RHEUMATOLOGY INTERNA	HCAPLUS
Silverberg, D	2002			US 2002065214 A1	
Thomas, C	2002	48	1066	CLINICAL CHEMISTRY	HCAPLUS

L108 ANSWER 3 OF 27 HCAPLUS COPYRIGHT 2005 ACS on STN

AN 2004:333839 HCAPLUS

DN 140:352406

TI Erythropoietin glycosylation and the modification of
protein structure and activity for therapeutic use

IN De Frees, Shawn; Zopf, David; Bayer, Robert; Bowe, Caryn; Hakes, David;
Chen, Xi

PA Neose Technologies, Inc., USA

SO PCT Int. Appl., 1018 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 15

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004033651	A2	20040422	WO 2003-US31974	20031008 <--
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RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
WO 2003031464	A2	20030417	WO 2002-US32263	20021009 <--
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,				

LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH,
 PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ,
 UA, UG, US, UZ, VN, YU, ZA, ZM, ZW
 RW: GH, GH, GM, GM, KE, KE, LS, LS, MW, MW, MZ, MZ, SD, SD, SL, SL,
 SZ, SZ, TZ, TZ, UG, UG, ZM, ZM, ZW, ZW, AM, AZ, BY, KG, KZ, MD,
 RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB,
 GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM,
 GA, GN, GQ

	US 2004137557	A1	20040715	US 2002-287994	20021105 <--
	CA 2501832	AA	20040422	CA 2003-2501832	20031008 <--
PRAI	WO 2002-US32263	A	20021009	<--	
	US 2002-287994	A	20021105	<--	
	US 2003-360770	A	20030106		
	US 2003-360779	A	20030219		
	US 2003-410945	A	20030409		
	US 2001-328523P	P	20011010	<--	
	US 2001-344692P	P	20011019	<--	
	US 2001-334233P	P	20011128	<--	
	US 2001-334301P	P	20011128	<--	
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	US 2002-404249P	P	20020816	<--	
	US 2002-407527P	P	20020828	<--	
	WO 2003-US31974	W	20031008		

AB The invention includes methods and compns. for remodeling a peptide mol., including the addition or deletion of one or more glycosyl groups to a peptide, and/or the addition of a modifying group to a peptide. Methods of modifying the structure and properties of **erythropoietin** by introduction of glycosidation are described. The method uses substitution variants of **erythropoietin** to introduce sites that can be **glycosylated** enzymically. The primary **glycosylation** may then be used to add further sugar residues. The glycosidation, which may include the introduction of N-acetylglucose, N-acetylgalactose, and sialic acid and mannosyl and fucosyl oligosaccharides. The carbohydrate moiety may in turn be modified by **PEGylation**. A biantennary glycosidated derivative of Epogen had 146% of the activity of the unmodified protein. The **glycosylated** proteins had longer serum half-lives than the unmodified protein and showed longer term effects on blood Hb levels.

IT **681860-67-3DP**, substitution derivs., **glycosylated**, **PEGylated**
 RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (amino acid sequence; **erythropoietin glycosylation**
 and modification of protein structure and activity for therapeutic use)
 RN **681860-67-3** HCAPLUS
 CN Erythropoietin (human 165-amino acid isoform) (9CI) (CA INDEX NAME)

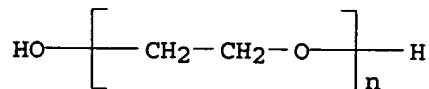
*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

IT **11096-26-7DP**, **Erythropoietin**, **glycosylated**
 derivs. **25322-68-3DP**, **Polyethylene glycol**,
 reaction products with **glycosylated erythropoietin**
 RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (**erythropoietin glycosylation** and modification of
 protein structure and activity for therapeutic use)
 RN **11096-26-7** HCAPLUS
 CN Erythropoietin (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

RN 25322-68-3 HCAPLUS

CN Poly(oxy-1,2-ethanediyl), α -hydro- ω -hydroxy- (9CI) (CA INDEX NAME)



IT 113427-24-0DP, Epogen, glycosylated derivs.

RL: PKT (Pharmacokinetics); PNU (Preparation, unclassified); BIOL (Biological study); PREP (Preparation)

(preparation and pharmacokinetics of; erythropoietin glycosylation and modification of protein structure and activity for therapeutic use)

RN 113427-24-0 HCAPLUS

CN 1-165-Erythropoietin (human clone λ HEPOFL13 protein moiety), glycoform α (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

L108 ANSWER 4 OF 27 HCAPLUS COPYRIGHT 2005 ACS on STN

AN 2004:287861 HCAPLUS

DN 140:320038

TI Chimeric and humanized anti-granulocyte antibodies, immunoconjugates and labeled antibodies for diagnosis and treatment of malignancy, infection and inflammation

IN Goldenberg, David M.; Hansen, Hans; Leung, Shui-on

PA Immunomedics, Inc., USA; McCall, John Douglas

SO PCT Int. Appl., 134 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2004029093	A2	20040408	WO 2003-GB4229	20030930 <--
	WO 2004029093	A3	20040603		
	W:				
	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
	RW:				
	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	CN 1542019	A	20041103	CN 2003-123054	20030429 <--
	CA 2500250	AA	20040408	CA 2003-2500250	20030930 <--
	EP 1546204	A2	20050629	EP 2003-751001	20030930 <--
	R:				
	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
PRAI	US 2002-414341P	P	20020930 <--		
	WO 2003-GB4229	W	20030930		

AB The present invention provides humanized, chimeric and human MN3 antibodies, fusion proteins, and fragments that bind NCA90 and NCA95 antigens. The antibodies, fusion proteins, and fragments thereof, as well

as combinations with other suitable antibodies, are useful for the treatment and diagnosis of granulocyte related disorders and diseases, such as leukemia.

IT 11096-26-7, Erythropoietin
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (chimeric and humanized anti-granulocyte antibodies, immunoconjugates and labeled antibodies for diagnosis and treatment of malignancy, infection and inflammation)
RN 11096-26-7 HCAPLUS
CN Erythropoietin (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

IT 7439-89-6, Iron, biological studies 15438-31-0, Iron(2+), biological studies 20074-52-6, Iron(3+), biological studies
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (chimeric and humanized anti-granulocyte antibodies, immunoconjugates and labeled antibodies for diagnosis and treatment of malignancy, infection and inflammation)
RN 7439-89-6 HCAPLUS
CN Iron (7CI, 8CI, 9CI) (CA INDEX NAME)

Fe

RN 15438-31-0 HCAPLUS
CN Iron, ion (Fe2+) (8CI, 9CI) (CA INDEX NAME)

Fe²⁺

RN 20074-52-6 HCAPLUS
CN Iron, ion (Fe3+) (8CI, 9CI) (CA INDEX NAME)

Fe³⁺

L108 ANSWER 5 OF 27 HCAPLUS COPYRIGHT 2005 ACS on STN

AN 2004:203692 HCAPLUS

DN 140:229921

TI Use of erythropoietin and analogs to treat disturbances of iron distribution in diabetes

IN Lehmann, Paul; Roeddiger, Ralf; Walter-Matsui, Ruth

PA F. Hoffmann-La Roche A.-G., Switz.

SO PCT Int. Appl., 31 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2004019972	A1	20040311	WO 2003-EP9194	20030820 <--
	W:			AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,	

GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM,
PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN,
TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES,
FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR,
BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
US 2004110679 A1 20040610 US 2003-634477 20030804 <--
CA 2496581 AA 20040311 CA 2003-2496581 20030820 <--
EP 1536823 A1 20050608 EP 2003-790911 20030820 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK
BR 2003013792 A 20050712 BR 2003-13792 20030820 <--
PRAI EP 2002-19100 A 20020829 <--
WO 2003-EP9194 W 20030820
AB The present invention relates to the use of **erythropoietin** for
the treatment of disturbances of iron distribution in diabetes.
IT **668496-68-2 668496-69-3**
RL: PAC (Pharmacological activity); PRP (Properties); THU (Therapeutic
use); BIOL (Biological study); USES (Uses)
(amino acid sequence; use of **erythropoietin (Epo)**
and analogs to treat disturbances of iron distribution in diabetes)
RN 668496-68-2 HCAPLUS
CN Erythropoietin (human 165-amino acids variant) (9CI) (CA INDEX NAME)
*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
RN 668496-69-3 HCAPLUS
CN Erythropoietin (human 166-amino acids variant) (9CI) (CA INDEX NAME)
*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
IT **11096-26-7, Erythropoietin 11096-26-7D,**
Erythropoietin, glycosylated and PEGylated
variants and conjugates
RL: PAC (Pharmacological activity); PRP (Properties); THU (Therapeutic
use); BIOL (Biological study); USES (Uses)
(use of **erythropoietin (Epo)** and analogs to treat
disturbances of iron distribution in diabetes)
RN 11096-26-7 HCAPLUS
CN Erythropoietin (9CI) (CA INDEX NAME)
*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
RN 11096-26-7 HCAPLUS
CN Erythropoietin (9CI) (CA INDEX NAME)
*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
IT **113427-24-0, Epoetin alfa 122312-54-3**
, Epoetin beta 209810-58-2,
Darbepoetin alfa
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
(Biological study); USES (Uses)
(use of **erythropoietin (Epo)** and analogs to treat
disturbances of iron distribution in diabetes)
RN 113427-24-0 HCAPLUS
CN 1-165-Erythropoietin (human clone λ HEPOFL13 protein moiety),
glycoform α (9CI) (CA INDEX NAME)
*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
RN 122312-54-3 HCAPLUS
CN 1-165-Erythropoietin (human clone λ HEPOFL13 protein moiety),

glycoform β (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

RN 209810-58-2 HCAPLUS

CN Erythropoietin [30-asparagine,32-threonine,87-valine,88-asparagine,90-threonine] (human) (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

RETABLE

Referenced Author (RAU)	Year (RPY)	VOL (RVL)	PG (RPG)	Referenced Work (RWK)	Referenced File
Harold, T	2002			US 6440932 B1	HCAPLUS
Hoffmann La Roche	2001			WO 0187329 A	HCAPLUS
Hoffmann La Roche	2003			WO 03025583 A	HCAPLUS

L108 ANSWER 6 OF 27 HCAPLUS COPYRIGHT 2005 ACS on STN

AN 2003:282607 HCAPLUS

DN 138:298131

TI **PEGylated and diglycosylated erythropoietin**
with improved pharmaceutical properties in induction of erythropoiesis

IN Tischer, Wilhelm

PA F. Hoffmann-La Roche Ag, Switz.

SO PCT Int. Appl., 22 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2003029291	A2	20030410	WO 2002-EP10556	20020920 <--
WO 2003029291	A3	20030724		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2003077753	A1	20030424	US 2002-241356	20020911 <--
US 6930086	B2	20050816		
CA 2460489	AA	20030410	CA 2002-2460489	20020920 <--
EP 1432802	A2	20040630	EP 2002-777160	20020920 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK				
CN 1558952	A	20041229	CN 2002-818752	20020920 <--
JP 2005509609	T2	20050414	JP 2003-532536	20020920 <--
PRAI EP 2001-122555	A	20010925	<--	
WO 2002-EP10556	W	20020920	<--	

AB The invention provides a new class of **EPO** muteins with improved pharmaceutical properties. The **EPO** muteins according to the invention have the in vivo biol. activity of causing bone marrow cells to increase production of reticulocytes and red blood cells. The invention provides an **erythropoietin** mutein which has retained the potential N-glycosylation sites at Asn24, Asn38, Asn83, is N-glycosylated at Asn38 and Asn83 but is not N-glycosylated at Asn24 and is preferably linked at the N-terminal amino group and/or the

ϵ -amino group of Lys20 to poly(ethylene glycol) group(s) (PEG), preferably to alkoxypoly(ethylene glycol) group(s), more preferably to lower methoxypoly(ethylene glycol) group(s). The muteins of this invention have the same uses as EPO. In particular, the muteins of this invention are useful to treat patients by stimulating the division and differentiation of committed erythroid progenitors in the bone marrow. The present invention also includes a method for the treatment of anemia in humans and the use of the muteins for the manufacturing of a pharmaceutical agent preferably for such treatment. The present invention also includes a method for preparing erythropoietin muteins according to the invention, which comprises the production of a glycosylated EPO fragment consisting of the amino acids 26-165-(EPO 26-165) and subsequent fusion of said fragment with a nonglycosylated but preferably PEGylated EPO fragment consisting of the amino acids 1-28 (EPO 1-28).

IT 510776-46-2DP, muteins 510776-47-3DP, muteins
RL: BPN (Biosynthetic preparation); PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(amino acid sequence; preparation of PEGylated and diglycosylated erythropoietin with improved pharmaceutical properties in induction of erythropoiesis)

RN 510776-46-2 HCAPLUS

CN Erythropoietin (human 165-amino acid isoform) (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

RN 510776-47-3 HCAPLUS

CN Erythropoietin (human 166-amino acid isoform) (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

IT 510776-48-4, 29-165-erythropoietin (human)
RL: RCT (Reactant); RACT (Reactant or reagent)
(amino acid sequence; preparation of PEGylated and diglycosylated erythropoietin with improved pharmaceutical properties in induction of erythropoiesis)

RN 510776-48-4 HCAPLUS

CN 29-165-erythropoietin (human) (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

IT 11096-26-7DP, Erythropoietin, muteins
RL: BPN (Biosynthetic preparation); PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of PEGylated and diglycosylated erythropoietin with improved pharmaceutical properties in induction of erythropoiesis)

RN 11096-26-7 HCAPLUS

CN Erythropoietin (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

L108 ANSWER 7 OF 27 HCAPLUS COPYRIGHT 2005 ACS on STN

AN 2002:869575 HCAPLUS

DN 137:346941

TI Method for improving the quality of life of patients by administration of erythropoietin (RhuEPO)

IN Zaharia, Veronica C.

PA USA

SO U.S. Pat. Appl. Publ., 4 pp., Cont.-in-part of U.S. Ser. No. 872,630.

CODEN: USXXCO
 DT Patent
 LA English
 FAN.CNT 3

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 2002169129	A1	20021114	US 2002-133545	20020426 <--
	US 5951996	A	19990914	US 1998-18815	19980204 <--
	US 6274158	B1	20010814	US 1999-335076	19990617 <--
	US 6521245	B1	20030218	US 2001-872630	20010601 <--
PRAI	US 1998-18815	A2	19980204	<--	
	US 1998-91598P	P	19980702	<--	
	US 1999-125253P	P	19990319	<--	
	US 1999-335076	A3	19990617	<--	
	US 2001-287206P	P	20010428	<--	
	US 2001-872630	A2	20010601	<--	

AB A method for providing various benefits with the administration of different quantities of **Erythropoietin**. The method provides for enhancing the of quality of life by administration of **Erythropoietin** before a substantial increases in Hb occurs. The improvement in quality of life is independent of the hemopoietic effect. In larger quantities the administration of **RhuEPO** leads to repair of vascular damage and leads to the redistribution of the **iron** trapped in storage organs, from where it cannot be used for red blood cell production, into the hemopoietic system leading to enhanced red blood cell production

IT **11096-26-7, Erythropoietin**
 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (method for improving the quality of life of patients by administration of **erythropoietin (RhuEPO)**)

RN 11096-26-7 HCAPLUS

CN Erythropoietin (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

IT **7439-89-6, Iron**, biological studies
 RL: BSU (Biological study, unclassified); BIOL (Biological study)
 (method for limiting chronic blood loss by administering **RhuEPO** to prevent **iron** loss and to increase Hb level, increased mean corpuscular Hb, and increased red blood cell hemoglobinization.)

RN 7439-89-6 HCAPLUS

CN Iron (7CI, 8CI, 9CI) (CA INDEX NAME)

Fe

L108 ANSWER 8 OF 27 HCAPLUS COPYRIGHT 2005 ACS on STN

AN 2002:785122 HCAPLUS

DN 138:298038

TI Long-term reversal of chronic anemia using a hypoxia-regulated **erythropoietin** gene therapy

AU Binley, Katie; Askham, Zoe; Iqball, Sharifah; Spearman, Hayley; Martin, Leigh; de Alwis, Mahesh; Thrasher, Adrian J.; Ali, Robin R.; Maxwell, Patrick H.; Kingsman, Susan; Naylor, Stuart

CS Oxford BioMedica (UK) Ltd, London, OX4 4GA, UK

SO Blood (2002), 100(7), 2406-2413

CODEN: BLOOAW; ISSN: 0006-4971

PB American Society of Hematology

DT Journal
 LA English
 AB Anemia is a common clin. problem, and there is much interest in its role in promoting left ventricular hypertrophy through increasing cardiac workload. Normally, red blood cell production is adjusted through the regulation of **erythropoietin (Epo)** production by the kidney. One important cause of anemia is relative deficiency of **Epo**, which occurs in most types of renal disease. Clin., this can be corrected by supplementation with recombinant **Epo**. Here the authors describe an oxygen-regulated gene therapy approach to treating homozygous **erythropoietin-SV40 T antigen (Epo-TAg)** mice with relative **erythropoietin** deficiency. The authors used vectors in which murine **Epo** expression was directed by an Oxford Biomedica hypoxia response element (OBHRE) or a constitutive cytomegalovirus (CMV) promoter. Both corrected anemia, but CMV-**Epo**-treated mice acquired fatal polycythemia. In contrast, OBHRE-**Epo** corrected the hematocrit level in anemic mice to a normal physiol. level that stabilized without resulting in polycythemia. Importantly, the OBHRE-**Epo** vector had no significant effect on the hematocrit of control mice. Homozygous **Epo-TAg** mice display cardiac hypertrophy, a common adaptive response in patients with chronic anemia. In the OBHRE-**Epo**-treated **Epo-TAg** mice, the authors observed a significant reversal of cardiac hypertrophy. The authors conclude that the OBHRE promoter gives rise to physiol. regulated **Epo** secretion such that the hematocrit level is corrected to healthy in anemic **Epo-TAg** mice. This establishes that a hypoxia regulatory mechanism similar to the natural mechanism can be achieved, and it makes **EPO** gene therapy more attractive and safer in clin. settings. The authors envisage that this control system will allow regulated delivery of therapeutic gene products in other ischemic settings.

IT 7439-89-6, Iron, biological studies
 RL: BSU (Biological study, unclassified); BIOL (Biological study) (long-term reversal of chronic anemia using hypoxia-regulated **erythropoietin** gene therapy)

RN 7439-89-6 HCAPLUS
 CN Iron (7CI, 8CI, 9CI) (CA INDEX NAME)

Fe

IT 11096-26-7, Erythropoietin
 RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (long-term reversal of chronic anemia using hypoxia-regulated **erythropoietin** gene therapy)

RN 11096-26-7 HCAPLUS
 CN Erythropoietin (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

RETABLE

Referenced Author (RAU)	Year (RPY)	VOL (RVL)	PG (RPG)	Referenced Work (RWK)	Referenced File
=====	=====	=====	=====	=====	=====
Anon	1989	2	20	Lancet	
Bachmann, S	1993	41	335	J Histochem Cytochem	HCAPLUS
Bartholomew, A	2001	12	1527	Hum Gene Ther	HCAPLUS
Beall, C	2000	7	534	Gene Ther	HCAPLUS
Binley, K	1999	6	1721	Gene Ther	HCAPLUS
Boast, K	1999	10	2197	Hum Gene Ther	HCAPLUS

Bohl, D	1998	92	1512	Blood	HCAPLUS
Bohl, D	2000	95	2793	Blood	HCAPLUS
Bohl, D	1997	3	299	Nat Med	HCAPLUS
Bron, D	2001	28	1	Semin Oncol	MEDLINE
Cowgill, L	1998	212	521	J Am Vet Med Assoc	HCAPLUS
Dalle, B	1999	6	157	Gene Ther	HCAPLUS
Erslev, A	1985	41	213	Nephron	MEDLINE
Eschbach, J	1989	35	134	Kidney Int	MEDLINE
Foley, R	1995	5	2024	J Am Soc Nephrol	MEDLINE
Goodnough, L	2000	96	823	Blood	HCAPLUS
Griffiths, L	2000	7	255	Gene Ther	HCAPLUS
Hamamori, Y	1995	95	1808	J Clin Invest	HCAPLUS
Jelkmann, W	1992	72	449	Physiol Rev	HCAPLUS
Kina, T	2000	109	280	Br J Haematol	HCAPLUS
Krystal, G	1983	11	649	Exp Hematol	HCAPLUS
Lynch, C	1999	1	493	Curr Opin Mol Ther	HCAPLUS
Maxwell, P	1993	44	1149	Kidney Int	HCAPLUS
Maxwell, P	1993	90	2423	Proc Natl Acad Sci U	HCAPLUS
Middleton, R	2001	12	1079	J Am Soc Nephrol	MEDLINE
Post, D		8	1801	Gene Ther	HCAPLUS
Raja, K	1997	96	248	Br J Haematol	HCAPLUS
Rendahl, K	1998	16	757	Nat Biotechnol	HCAPLUS
Rinsch, C	1997	8	1881	Hum Gene Ther	HCAPLUS
Rudich, S	2000	90	102	J Surg Res	HCAPLUS
Semenza, G	2000	14	1983	Genes Dev	HCAPLUS
Seppen, J	2001	98	594	Blood	HCAPLUS
Serguera, C	1999	10	375	Hum Gene Ther	HCAPLUS
Setoguch, Y	1994	84	2946	Blood	
Villeval, J	1994	84	928	Blood	HCAPLUS
Wang, G	1993	90	4304	Proc Natl Acad Sci U	HCAPLUS
Wang, G	1995	92	5510	Proc Natl Acad Sci U	HCAPLUS
Ye, X	1999	283	88	Science	HCAPLUS
Zhang, X	1999	10	2527	Hum Gene Ther	HCAPLUS
Zhou, S	1998	5	665	Gene Ther	HCAPLUS

L108 ANSWER 9 OF 27 HCAPLUS COPYRIGHT 2005 ACS on STN

AN 2002:761224 HCAPLUS

DN 137:288375

TI The correction of anemia in severe resistant heart failure with **erythropoietin** and intravenous **iron** prevents the progression of both the heart and the renal failure and markedly reduces hospitalization

AU Silverberg, D. S.; Wexler, D.; Blum, M.; Tchebiner, J.; Sheps, D.; Keren, G.; Schwartz, D.; Baruch, R.; Yachnin, T.; Shaked, M.; Zubkov, A.; Steinbruch, S.; Iaina, A.

CS Department of Nephrology and Cardiology and Congestive Heart Failure Unit and Medical Department B, Tel Aviv Medical Center, Tel Aviv-Jaffa, 64239, Israel

SO Clinical Nephrology (2002), 58(1, Suppl. 1), S37-S45
CODEN: CLNHBI; ISSN: 0301-0430

PB Dustri-Verlag Dr. Karl Feistle

DT Journal; General Review

LA English

AB A review. Both Congestive Heart Failure (CHF) and Chronic Renal Failure (CRF) are increasing steadily in the community. We propose that there is a vicious circle established whereby CHF and CRF both cause anemia and the anemia then worsens both the CHF and CRF causing more anemia and so on. We call this the Cardio Renal Anemia (CRA) syndrome. By the combination of active treatment of the CHF and control of the anemia with s.c. **erythropoietin** and i.v. **iron**, the progression of both

the CHF and the CRF can be slowed or stopped in most cases, the quality of life improved and the need for recurrent hospitalization reduced. This will involve cooperation between internists, cardiologists, and nephrologists to allow early and maximal therapy of both the CHF and the anemia.

IT 7439-89-6, Iron, biological studies 11096-26-7

, Erythropoietin

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(erythropoietin and i.v. iron correction of anemia

in severe resistant heart failure patients prevents progression of both heart and renal failure and markedly reduces hospitalization)

RN 7439-89-6 HCAPLUS

CN Iron (7CI, 8CI, 9CI) (CA INDEX NAME)

Fe

RN 11096-26-7 HCAPLUS

CN Erythropoietin (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

RETABLE

Referenced Author (RAU)	Year (RPY)	VOL (RVL)	PG (RPG)	Referenced Work (RWK)	Referenced File
Al-Ahmad, A	2001	38	955	J Am Coll Cardiol	MEDLINE
Anand, I	1993	70	357	Br Heart J	MEDLINE
Bosman, D	2001	24	495	Diabetes Care	MEDLINE
Capes, S	2000	23	377	Diabetes Care	HCAPLUS
Carson, J	1995	170	328	Amer J Surg	
Cowie, M	1997	18	208	Eur Heart J	HCAPLUS
Dries, D	2001	38	421	J Am Coll Cardiology	MEDLINE
Felker, G	2001	17		Circulation	
Fine, L	1998	53	s74	Kidney Int	
Fine, L	2000	57	S22	Kidney Int	
Fishbane, S	1995	26	41	Am J Kidney Dis	MEDLINE
Foley, R	1996	28	53	Am J Kidney Dis	MEDLINE
Foley, R	1995	47	186	Kidney Int	MEDLINE
Goodnough, L	2001	345	1272	N Engl J Med	MEDLINE
Hampl, H	1985	39	102	Nephron	MEDLINE
He, J	2001	161	996	Arch Int Med	MEDLINE
Herrera-Garza, E	1999	115	1170	Chest	MEDLINE
Hillege, H	1999	10	A384	J Am Soc Nephrol	
Holland, D	2000	15	650	Nephrol Dial Transpl	MEDLINE
Iverson, P	2002	282	R166	Am J Physiol Regul I	
Jafar, T	2001	60	1131	Kidney Int	HCAPLUS
Johnson, D	1996	5	186	Current Opinion in N	MEDLINE
Jungers, P	2001	16	307	Nephrol Dialysis Tra	HCAPLUS
Katz, A	1994	121	363	Ann Intern Med	HCAPLUS
Knight, E	1999	138	849	Am Ht J	MEDLINE
Kratz, A	1998	339	1063	N Engl J Med	MEDLINE
Kuriyama, S	1997	77	176	Nephron	HCAPLUS
Linde, T	1996	30	115	Scand J Urol Nephrol	MEDLINE
Longenecker, J	2000	11	520	J Am Soc Nephrol	MEDLINE
Macdougall, I	1996	50	1694	Kidney Int	HCAPLUS
Macdougall, I	1999	14	1836	Nephrol Dial Transpl	MEDLINE
Major, A	1997	98	292	Brit J Haematol	HCAPLUS
Mancini, D	2000	101	1080	Circulation	MEDLINE

Mancini, D	2001	17		Circulation	
McAlister, F	1999	138	87	Amer Heart J	MEDLINE
Means, R	1999	70	7	Int J Hematol	
Miller, L	2001	19	547	Cardiology Clinics	MEDLINE
Mosterd, A	2001	22	1318	Eur Heart J	MEDLINE
O'Connell, J	2000	23	6	Clin Cardiol	
Packer, M	1999	83	1	Am J Cardiol	
Perry, H	1995	25	587	Hypertension	
Petrie, M	2001	22	1978	Eur Heart J	MEDLINE
Philbin, E	2000	109	605	Amer J Med	HCAPLUS
Rich, M	1995	333	1190	N Engl J Med	MEDLINE
Roth, D	1994	24	777	Am J Kidney Dis	MEDLINE
Silagy, C	1993	54	84	Clin Pharm Therapy	MEDLINE
Silverberg, D	2001	23	1	Clin Lab Haem	MEDLINE
Silverberg, D	2000	35	1737	J Am Coll Cardiol	HCAPLUS
Silverberg, D	2001	37	1775	J Am Coll Cardiol	HCAPLUS
Silverberg, D	1996	72	413	Nephron	HCAPLUS
Silverberg, D	2001	21	S236	Periton Dial Int	
Sommerburg, O	2000	53	S23	Clin Nephrol	
Sunder-Plassmann, G	2001	38	S20	Am J Kidney Diseases	
Tong, E	2001	21	190	Seminars in Nephrolo	HCAPLUS
Tsuyuki, R	2001	161	2337	Archives Int Med	MEDLINE
US Renal Data System	2001			Annual Data Report	
Vaziri, N	2001	38	1	Am J Kidney Dis	HCAPLUS
Wahr, J	1998	81	10	Br J Anaest	
Winkler, A	1999	16	813	Diabetes Medicine	MEDLINE
Wisniacki, N	2001	85	P4	Heart	
Wu, W	2001	345	1230	N Engl J Med	MEDLINE
Yoshida, H	1998	53	880	Kidney Int	MEDLINE

L108 ANSWER 10 OF 27 HCAPLUS COPYRIGHT 2005 ACS on STN

AN 2002:487418 HCAPLUS

DN 137:68127

TI Erythropoietin conjugates

IN Burg, Josef; Engel, Alfred; Franze, Reinhard; Hilger, Bernd; Schurig, Hartmut Ernst; Tischer, Wilhelm; Wozny, Manfred

PA F. Hoffmann-La Roche Ag, Switz.

SO PCT Int. Appl., 40 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2002049673	A2	20020627	WO 2001-EP14434	20011208 <--
	WO 2002049673	A3	20030123		
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	CA 2431964	AA	20020627	CA 2001-2431964	20011208 <--
	AU 2002033230	A5	20020701	AU 2002-33230	20011208 <--
	EP 1345628	A2	20030924	EP 2001-984811	20011208 <--
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				

BR 2001016381	A	20040225	BR 2001-16381	20011208 <--
JP 2004525097	T2	20040819	JP 2002-551010	20011208 <--
CN 1527726	A	20040908	CN 2001-820609	20011208 <--
US 2002115833	A1	20020822	US 2001-14363	20011211 <--
ZA 2003004647	A	20040913	ZA 2003-4647	20030613 <--
PRAI EP 2000-127891	A	20001220	<--	
WO 2001-EP14434	W	20011208	<--	

AB The present invention refers to **conjugates of erythropoietin with poly(ethylene glycol)** comprising an **erythropoietin** glycoprotein having an N-terminal α -amino group and having the in vivo biol. activity of causing bone marrow cells to increase production of reticulocytes and red blood cells and selected from the group consisting of human **erythropoietin** and analogs thereof which have the sequence of human **erythropoietin** modified by the addition of from 1 to 6 **glycosylation** sites or a rearrangement of at least one **glycosylation** site; said glycoprotein being covalently linked to one **poly(ethylene glycol)** group of the formula $-\text{CO}-(\text{CH}_2)_x-(\text{OCH}_2\text{CH}_2)_m-\text{OR}$ with the $-\text{CO}$ of the **poly(ethylene glycol)** group forming an amide bond with said N-terminal α -amino group; wherein R is lower alkyl; x is 2 or 3; and m is from about 450 to about 1350.

IT **11096-26-7DP, Erythropoietin, conjugates**
 RL: PNU (Preparation, unclassified); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (glycosylation site-augmented human **erythropoietin** conjugates with PEG)

RN 11096-26-7 HCAPLUS
 CN Erythropoietin (9CI) (CA INDEX NAME)

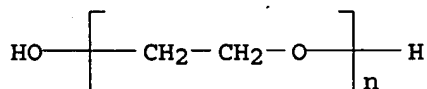
*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

IT **11096-26-7, Erythropoietin 25322-68-3D, Polyethylene glycol, erythropoietin conjugates**
 RL: RCT (Reactant); RACT (Reactant or reagent)
 (glycosylation site-augmented human **erythropoietin** conjugates with PEG)

RN 11096-26-7 HCAPLUS
 CN Erythropoietin (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

RN 25322-68-3 HCAPLUS
 CN Poly(oxy-1,2-ethanediyl), α -hydro- ω -hydroxy- (9CI) (CA INDEX NAME)



L108 ANSWER 11 OF 27 HCAPLUS COPYRIGHT 2005 ACS on STN

AN 2002:409245 HCAPLUS

DN 136:380106

TI Method of treating congestive heart failure with **erythropoietin** and an **iron** compound

IN Iaina, Adrian; Wexler, Dov; Silverberg, Donald S.

PA Israel

SO U.S. Pat. Appl. Publ., 3 pp.

CODEN: USXXCO

DT Patent
LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 2002065214	A1	20020530	US 2000-725161	20001129 <--
PRAI	US 2000-725161		20001129	<--	

AB A method of treating congestive heart failure in a subject suffering therefrom, comprising administering **erythropoietin** and i.v. administering an i.v. administrable **iron** compound to the subject. The **iron** is preferably administered in the form of a complex of a ferric hydroxide with **erythropoietin**.

IT **11096-26-7, Erythropoietin**
 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (method of treating congestive heart failure with **erythropoietin** and an **iron** compound)

RN 11096-26-7 HCAPLUS

CN Erythropoietin (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

L108 ANSWER 12 OF 27 HCAPLUS COPYRIGHT 2005 ACS on STN

AN 2001:850963 HCAPLUS

DN 136:11065

TI New pharmaceutical composition

IN Papadimitriou, Apollon

PA F. Hoffmann-La Roche A.-G., Switz.

SO PCT Int. Appl., 64 pp.

CODEN: PIXXD2

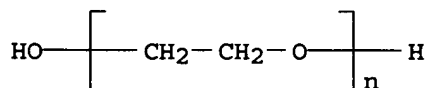
DT Patent

LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2001087329	A1	20011122	WO 2001-EP5187	20010508 <--
	W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CO, CU, CZ, DE, DK, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	CA 2408685	AA	20011122	CA 2001-2408685	20010508 <--
	BR 2001010914	A	20030211	BR 2001-10914	20010508 <--
	EP 1311285	A2	20030521	EP 2001-943331	20010508 <--
	EP 1311285	B1	20050323		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
	JP 2003533487	T2	20031111	JP 2001-583796	20010508 <--
	NZ 522030	A	20041126	NZ 2001-522030	20010508 <--
	AT 291436	E	20050415	AT 2001-943331	20010508 <--
	EP 1525889	A1	20050427	EP 2005-984	20010508 <--
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, CY, TR				
	US 2002037841	A1	20020328	US 2001-853731	20010511 <--
	ZA 2002008500	A	20040128	ZA 2002-8500	20021021 <--

NO 2002005450 A 20021114 NO 2002-5450 20021114 <--
 US 2004147431 A1 20040729 US 2004-780297 20040217 <--
 PRAI EP 2000-110355 A 20000515 <--
 EP 2001-943331 A3 20010508 <--
 WO 2001-EP5187 W 20010508 <--
 US 2001-853731 A1 20010511 <--
 AB The present invention relates to a liquid pharmaceutical composition comprising an **erythropoietin** protein, a multiple charged inorg. anion in a pharmaceutically acceptable buffer suitable to keep the solution pH in the range from about 5.5 to about 7.0, and optionally one or more pharmaceutically acceptable excipients. This composition is especially useful for the prophylaxis and treatment of diseases related to erythropoiesis.
 IT **96024-34-9P, Erythropoietin** (human clone λ HEPOFL13 protein moiety reduced) **134547-95-8P, 1-165-Erythropoietin** (human clone λ HEPOFL13 protein moiety reduced)
 RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (amino acid sequence; stabilized **erythropoietin** pharmaceutical composition)
 RN 96024-34-9 HCAPLUS
 CN Erythropoietin (human clone λ HEPOFL13 protein moiety reduced) (9CI)
 (CA INDEX NAME)
 *** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
 RN 134547-95-8 HCAPLUS
 CN 1-165-Erythropoietin (human clone λ HEPOFL13 protein moiety reduced) (9CI) (CA INDEX NAME)
 *** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
 IT **11096-26-7P, Erythropoietin**
 RL: BPN (Biosynthetic preparation); PEP (Physical, engineering or chemical process); PRP (Properties); PUR (Purification or recovery); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)
 (stabilized **erythropoietin** pharmaceutical composition)
 RN 11096-26-7 HCAPLUS
 CN Erythropoietin (9CI) (CA INDEX NAME)
 *** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
 IT **25322-68-3D, Polyethylene glycol, protein conjugates**
 RL: PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
 (stabilized **erythropoietin** pharmaceutical composition)
 RN 25322-68-3 HCAPLUS
 CN Poly(oxy-1,2-ethanediyl), α -hydro- ω -hydroxy- (9CI) (CA INDEX NAME)



RETABLE

Referenced Author (RAU)	Year (RPY)	VOL (RVL)	PG (RPG)	Referenced Work (RWK)	Referenced File
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Author	Year	Volume	Page	Work	File
Alkermes	1996			WO 9640073 A	HCAPLUS
Chugai Seiyaku Kk	1986			EP 0178665 A	HCAPLUS
Chugai Seiyaku Kk	1986			GB 2171304 A	HCAPLUS
Chugai Seiyaku Kk	1999			EP 0909564 A	HCAPLUS
Woog, H	1991			US 4992419 A	HCAPLUS

L108 ANSWER 13 OF 27 HCAPLUS COPYRIGHT 2005 ACS on STN

AN 2001:715798 HCAPLUS

DN 136:15603

TI **Erythropoietin** therapy and preoperative autologous blood donation in children undergoing open heart surgery

AU Sonzogni, V.; Crupi, G.; Poma, R.; Annechino, F.; Ferri, F.; Filisetti, P.; Bellavita, P.

CS Department of Anesthesiology, Ospedali Riuniti di Bergamo, Bergamo, Italy

SO British Journal of Anaesthesia (2001), 87(3), 429-434

CODEN: BJANAD; ISSN: 0007-0912

PB Oxford University Press

DT Journal

LA English

AB We assessed the feasibility and efficacy of s.c. **erythropoietin** alpha (**EPO**) therapy and preoperative autologous blood donation (ABD) in children undergoing open heart surgery. Thirty-nine children were treated consecutively with **EPO** (100 U kg⁻¹ s.c. three times a week in the 3 wk preceding the operation and i.v. on the day of surgery) and two ABDs were made (Group 1). As controls to compare transfusion requirements, 39 consecutive age-matched patients who had undergone open heart surgery during the two preceding years were selected (Group 2). In a mean time of 20 (SD 5) days, 96% of scheduled ABDs were performed and only three mild vasovagal reactions were observed. The mean volume of autologous red blood cells (RBC) collected was 6 (1) ml kg⁻¹ and the mean volume of autologous RBC produced as a result of **EPO** therapy before surgery was 7 (3) ml kg⁻¹, corresponding to a 28 (11)% increase in circulating RBC volume. The mean volume of autologous RBC collected was not different from that produced [6 (1) vs. 7 (3) ml kg⁻¹, P=0.4]. Allogenic blood was administered to three out of 39 children in Group 1 (7.7%) and to 24 out of 39 (61.5%) in Group 2. Treatment with s.c. **EPO** increases the amount of autologous blood that can be collected and minimizes allogenic blood exposure in children undergoing open heart surgery.

IT 113427-24-0, **Eprex**

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(**erythropoietin** therapy and preoperative autologous blood donation in children undergoing open heart surgery)

RN 113427-24-0 HCAPLUS

CN 1-165-Erythropoietin (human clone λ HEPOFL13 protein moiety), glycoform α (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

RETABLE

Referenced Author (RAU)	Year (RPY)	VOL (RVL)	PG (RPG)	Referenced Work (RWK)	Referenced File
Adamson, J	1994	115	7	Surgery	MEDLINE
Anon	1988	260	2700	Consensus conference	
Baron, J	1997	33	64	Semin Hematol	
Beguin, Y	1999	84	541	Haematologica	HCAPLUS
Chaplin, H	1953	32	1309	J Clin Invest	
Cooley, D	1995	170	53	Am J Surg	
Coyle, D	2000	18	161	Pharmacoeconomics	MEDLINE

Despotis, G	1999	11	84	Semin Thorac Cardiovasc	MEDLINE
Fukahara, K	1997	114	504	J Thoroc Cardiovasc	MEDLINE
Goodnough, L	1994	101	354	Am J Clin Pathol	MEDLINE
Goodnough, L	1995	60	473	Ann Thorac Surg	MEDLINE
Goodnough, L	1990	115	28	J Lab Clin Med	MEDLINE
Goodnough, L	1989	321	1163	N Engl J Med	MEDLINE
Goodnough, L	1997	336	933	N Engl J Med	MEDLINE
Goodnough, L	1999	340	438	N Engl J Med	MEDLINE
Goodnough, L	1992	32	441	Transfusion	MEDLINE
Goodnough, L	1993	33	944	Transfusion	MEDLINE
Goodnough, L	1994	34	66	Transfusion	MEDLINE
Guay, J	1996	62	1955	Ann Thorac Surg	MEDLINE
Klapper, E	1995	110	1594	J Thorac Cardiovasc	MEDLINE
Krantz, S	1991	77	419	Blood	HCAPLUS
Marchetti, M	2000	40	673	Transfusion	MEDLINE
Masuda, M	1995	60	1694	Ann Thorac Surg	MEDLINE
Mayer, M	1996	70	224	Vax Sang	MEDLINE
McVay, P	1990	30	249	Transfusion	MEDLINE
Mercuriali, F	1993	30	17	Semin Hematol	
Price, T	1996	36	29	Transfusion	MEDLINE
Robertie, P	1990	28	197	Int Anaesthesiol Cli	MEDLINE
Russell, S	1949	24	88	Arch Dis Child	
Schmoeckel, M	1993	41	363	Thorac Cardiovasc Su	
Shaddy, R	1995	149	322	Arch Pediatr Adolesc	MEDLINE
Shimpo, H	1997	111	1565	Chest	HCAPLUS
Sowade, O	1997	89	411	Blood	HCAPLUS
Tasaki, T	1994	66	188	Vax Sang	MEDLINE
Walpoth, B	1997	33	75	Semin Hematol	
Watanabe, Y	1992	54	479	Ann Thorac Surg	MEDLINE
Welch, H	1992	116	393	Ann Intern Med	MEDLINE
Williams, G	1999	89	57	Anesth Analg	MEDLINE

L108 ANSWER 14 OF 27 HCAPLUS COPYRIGHT 2005 ACS on STN

AN 2001:505221 HCAPLUS

DN 135:267638

TI The effect of correction of mild anemia in severe, resistant congestive heart failure using subcutaneous erythropoietin and intravenous iron: a randomized controlled study

AU Silverberg, Donald S.; Wexler, Dov; Sheps, David; Blum, Miriam; Keren, Gad; Baruch, Ron; Schwartz, Doron; Yachnin, Tatyana; Steinbruch, Shoshana; Shapira, Itzhak; Laniado, Shlomo; Iaina, Adrian

CS Department of Nephrology and Cardiology and Congestive Heart Failure, Tel Aviv Medical Center, Tel Aviv-Jaffa, Israel

SO Journal of the American College of Cardiology (2001), 37(7), 1775-1780

CODEN: JACCDI; ISSN: 0735-1097

PB Elsevier Science Inc.

DT Journal

LA English

AB This is a randomized controlled study of anemic patients with severe congestive heart failure (CHF) to assess the effect of correction of the anemia on cardiac and renal function and hospitalization. Although mild anemia occurs frequently in patients with CHF, there is very little information about the effect of correcting it with erythropoietin (EPO) and i.v. iron. Thirty-two patients with moderate to severe CHF (New York Heart Association [NYHA] class III to IV) who had a left ventricular ejection fraction (LVEF) of $\leq 40\%$ despite maximally tolerated doses of CHF medications and whose Hb levels were persistently between 10.0 and 11.5 g% were randomized into two groups. Group A (16 patients) received s.c. EPO and IV iron to

increase the level of Hb to at least 12.5 g%. In Group B (16 patients) the anemia was not treated. The doses of all the CHF medications were maintained at the maximally tolerated levels except for oral and i.v. (IV) furosemide, whose doses were increased or decreased according to the clin. need. Over a mean of 8.2 ± 2.6 mo, four patients in Group B and none in Group A died of CHF-related illnesses. The mean NYHA class improved by 42.1% in A and worsened by 11.4% in B. The LVEF increased by 5.5% in A and decreased by 5.4% in B. The serum creatinine did not change in A and increased by 28.6% in B. The need for oral and IV furosemide decreased by 51.3% and 91.3% resp. in A and increased by 28.5% and 28.0% resp. in B. The number of days spent in hospital compared with the same period of time before entering the study decreased by 79.0% in A and increased by 57.6% in B. When anemia in CHF is treated with EPO and IV iron, a marked improvement in cardiac and patient function is seen, associated with less hospitalization and renal impairment and less need for diuretics.

IT 11096-26-7, Erythropoietin

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(effect of correction of mild anemia in congestive heart failure using s.c. erythropoietin and i.v. iron)

RN 11096-26-7 HCAPLUS

CN Erythropoietin (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

RETABLE

Referenced Author (RAU)	Year (RPY)	VOL (RVL)	PG (RPG)	Referenced Work (RWK)	Referenced File
Al-Ahmad, A	2000	11	137A	J Am Soc Nephrol	
Alexander, M	1999	137	919	Am Heart J	MEDLINE
Ali, A	1999	138	1133	Am Heart J	MEDLINE
Anand, I	1993	70	357	Br Heart J	MEDLINE
Anon	1997	30	S193	Am J Kidney Dis	
Bardaji, A	1998	32	970	Am J Kid Dis	MEDLINE
Carson, J	1995	170	32	Am J Surg	
Carson, J	1996	348	1055	Lancet	MEDLINE
De Simone, G	2000	101	152	Circulation	MEDLINE
Fine, L	1998	53	S74	Kidney Intl	
Fishbane, S	1995	26	41	Am J Kidney Dis	MEDLINE
Foley, R	1996	28	53	Am J Kidney Dis	MEDLINE
Ghali, J	1988	148	2013	Arch Intern Med	MEDLINE
Goldberg, N	1992	124	424	Am Heart J	MEDLINE
Haber, H	1991	324	353	N Engl J Med	MEDLINE
Harnett, J	1995	47	884	Kidney Int	MEDLINE
Hebert, P	1997	155	1618	Am J Respir Crit Car	MEDLINE
Hillege, H	1999	10	A384	J Am Soc Nephrol	
Jensen, J	1993	233	125	J Int Med	MEDLINE
Kannel, W	1987	8	23	Eur Heart J	
Knight, E	1999	138	849	Am Heart J	MEDLINE
Kuriyama, S	1996	9	426	Am J Hypertension	HCAPLUS
Locatelli, F	1998	13	1642	Nephrol Dial Transpl	MEDLINE
Low-Friedrich, I	1991	11	54	Am J Nephrol	MEDLINE
Ma, J	1999	10	610	J Am Soc Nephrol	MEDLINE
Macdougall, I	1996	50	1694	Kidney Int	HCAPLUS
Magri, P	1998	98	2849	Circulation	HCAPLUS
Maschio, G	1995	10	74	Nephrol Dial Transpl	
Opasich, C	1996	78	354	Am J Cardiol	MEDLINE
Packer, M	1999	83	1	Am J Cardiol	

Perry, H	1995	25	587	Hypertension	
Rich, M	1996	44	638	J Am Geriatr Soc	MEDLINE
Silverberg, D	2000	35	1737	J Am Coll Cardiol	HCAPLUS
Silverberg, D	1999	55	579	Kidney Int	
Silverberg, D	1996	72	413	Nephron	HCAPLUS
Sowade, O	1997	129	97	J Lab Clin Med	HCAPLUS
Stefanski, A	1996	50	1321	Kidney Int	MEDLINE
Wackers, F	1979	43	1159	Am J Cardiol	MEDLINE
Wald, M	1996	167	461	J Cell Physiol	HCAPLUS
Wald, M	1995	71	190	Nephron	HCAPLUS
Wu, H	1999	126	3597	Development	HCAPLUS
Xia, H	1999	10	1309	J Am Soc Nephrol	MEDLINE
Yoshida, H	1998	53	880	Kidney Int	MEDLINE

L108 ANSWER 15 OF 27 HCAPLUS COPYRIGHT 2005 ACS on STN

AN 2001:31360 HCAPLUS

DN 134:105827

TI Erythropoietin derivatives

IN Burg, Josef; Hilger, Bernd; Josel, Hans-Peter

PA F. Hoffmann-La Roche A.-G., Switz.

SO PCT Int. Appl., 40 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2001002017	A2	20010111	WO 2000-EP6009	20000628 <--
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2378533	AA	20010111	CA 2000-2378533	20000628 <--
US 6340742	B1	20020122	US 2000-604871	20000628 <--
EP 1196443	A2	20020417	EP 2000-951312	20000628 <--
EP 1196443	B1	20040526		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
BR 2000012138	A	20020507	BR 2000-12138	20000628 <--
TR 200103782	T2	20020521	TR 2001-200103782	20000628 <--
JP 2003503464	T2	20030128	JP 2001-507507	20000628 <--
AU 768452	B2	20031211	AU 2000-64299	20000628 <--
NZ 516170	A	20040227	NZ 2000-516170	20000628 <--
AT 267840	E	20040615	AT 2000-951312	20000628 <--
RU 2232163	C2	20040710	RU 2002-102232	20000628 <--
PT 1196443	T	20040930	PT 2000-951312	20000628 <--
ES 2220501	T3	20041216	ES 2000-951312	20000628 <--
ZA 2001010097	A	20030307	ZA 2001-10097	20011207 <--
NO 2001006304	A	20020219	NO 2001-6304	20011221 <--
PRAI US 1999-142243P	P	19990702	<--	
US 1999-147452P	P	19990805	<--	
US 1999-151454P	P	19990830	<--	
WO 2000-EP6009	W	20000628	<--	

AB Erythropoietin glycoprotein conjugates are disclosed, said conjugates comprise an erythropoietin

glycoprotein having at least one free amino group and having the in vivo biol. activity of causing bone marrow cells to increase production of reticulocytes and red blood cells and selected from the group consisting of human **erythropoietin** and analogs thereof which have the primary structure of human **erythropoietin** modified by the addition of from 1 to 6 **glycosylation** sites or by the rearrangement of at least one **glycosylation** site; said glycoprotein being covalently linked to form one to three lower-alkoxy **poly(ethylene glycol)** groups, each **poly(ethylene glycol)** group being covalently linked to the glycoprotein via a linker of the formula -C(O)-X-S-Y- with the C(O) of the linker forming an amide bond with one of said amino groups, wherein X and Y are as defined in the description and claims, the average mol. weight of each **poly(ethylene glycol)** moiety is from about 20 kilodaltons to about 40 kilodaltons, and the mol. weight of the **conjugate** is from about 51 kilodaltons to about 175 kilodaltons.

IT 96024-34-9, **Erythropoietin** (human clone λ HEPOFL13 protein moiety reduced) 134547-95-8, 1-165-**Erythropoietin** (human clone λ HEPOFL13 protein moiety reduced)

RL: BOC (Biological occurrence); BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); OCCU (Occurrence); PROC (Process); USES (Uses)

(amino acid sequence; **erythropoietin** derivs. for increasing production of erythrocytes and reticulocytes)

RN 96024-34-9 HCAPLUS

CN Erythropoietin (human clone λ HEPOFL13 protein moiety reduced) (9CI)
(CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

RN 134547-95-8 HCAPLUS

CN 1-165-Erythropoietin (human clone λ HEPOFL13 protein moiety reduced)
(9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

IT 11096-26-7D, **Erythropoietin, conjugates**

25322-68-3D, **erythropoietin conjugates**

RL: PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)

(**erythropoietin** derivs. for increasing production of erythrocytes and reticulocytes)

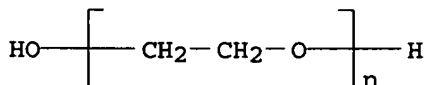
RN 11096-26-7 HCAPLUS

CN Erythropoietin (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

RN 25322-68-3 HCAPLUS

CN Poly(oxy-1,2-ethanediyl), α -hydro- ω -hydroxy- (9CI) (CA INDEX NAME)



L108 ANSWER 16 OF 27 HCAPLUS COPYRIGHT 2005 ACS on STN

AN 2001:10610 HCAPLUS

DN 134:91083

TI **Erythropoietin derivatives for increasing bone marrow production**
of reticulocytes and erythrocytes

IN Bailon, Pascal Sebastian

PA F. Hoffmann-La Roche A.-G., Switz.

SO Eur. Pat. Appl., 16 pp.

CODEN: EPXXDW

DT Patent

LA English

FAN.CNT 5

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 1064951	A2	20010103	EP 2000-113115	20000628 <--
	EP 1064951	A3	20020320		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
	US 6583272	B1	20030624	US 2000-604938	20000627 <--
	CA 2310536	AA	20010102	CA 2000-2310536	20000628 <--
	NO 2000003372	A	20010103	NO 2000-3372	20000628 <--
	TR 200001956	A2	20010122	TR 2000-200001956	20000628 <--
	HR 2000000436	A1	20010630	HR 2000-436	20000628 <--
	AU 736067	B2	20010726	AU 2000-42744	20000628 <--
	AU 2000042744	A5	20010104		
	NZ 505454	A	20011221	NZ 2000-505454	20000628 <--
	ZA 2000003282	A	20010102	ZA 2000-3282	20000629 <--
	CN 1280137	A	20010117	CN 2000-107889	20000629 <--
	SG 92717	A1	20021119	SG 2000-3658	20000629 <--
	DE 10031839	A1	20010201	DE 2000-10031839	20000630 <--
	GB 2353281	A1	20010221	GB 2000-16205	20000630 <--
	GB 2353281	B2	20040609		
	BG 104570	A	20010928	BG 2000-104570	20000630 <--
	IT 2000MI1479	A1	20011231	IT 2000-MI1479	20000630 <--
	IT 1318606	B1	20030827		
	ES 2191511	A1	20030901	ES 2000-1625	20000630 <--
	ES 2191511	B1	20050101		
	GB 2393960	A1	20040414	GB 2004-86	20000630 <--
	GB 2393960	B2	20040804		
	FR 2795734	A1	20010105	FR 2000-8609	20000703 <--
	JP 2001064300	A2	20010313	JP 2000-201525	20000703 <--
	BR 2000002276	A	20011211	BR 2000-2276	20000703 <--
	US 2003120045	A1	20030626	US 2002-293551	20021114 <--
	JP 2004155787	A2	20040603	JP 2003-419520	20031217 <--
PRAI	US 1999-142254P	P	19990702	<--	
	US 1999-150225P	P	19990823	<--	
	US 1999-151548P	P	19990831	<--	
	US 1999-166151P	P	19991117	<--	
	US 2000-604938	A1	20000627	<--	
	GB 2000-16205	A3	20000630	<--	
	JP 2000-201525	A3	20000703	<--	

AB The present invention refers to **conjugates of erythropoietin with poly(ethylene glycol)** comprising an **erythropoietin glycoprotein** having at least one free amino group and having the in vivo biol. activity of causing bone marrow cells to increase production of reticulocytes and red blood cells and selected from the group consisting of human **erythropoietin** and analogs thereof which have sequence of human **erythropoietin** modified by the addition of 1-6 **glycosylation** sites or a rearrangement of at least one **glycosylation** site; said glycoprotein being covalently linked to "n" **poly(ethylene glycol)** groups of the formula -CO-(CH₂)_x(OCH₂CH₂)_m-OR with the carbonyl of each **poly(**

ethylene glycol) group forming an amide bond with one of said amino groups; wherein R is lower alkyl; x = 2 or 4; m = 450-900; n = 1-3; and n and m are chosen so that the mol. weight of the conjugate minus the erythropoietin glycoprotein is 20-100 kDa.

IT 134547-95-8P, 1-165-Erythropoietin (human clone λ HEPOFL13 protein moiety reduced)
 RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (amino acid sequence; erythropoietin derivs. for increasing bone marrow production of reticulocytes and erythrocytes)
 RN 134547-95-8 HCAPLUS
 CN 1-165-Erythropoietin (human clone λ HEPOFL13 protein moiety reduced) (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

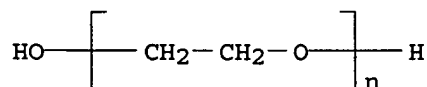
IT 11096-26-7D, Erythropoietin, polyethylene glycol conjugates 221039-34-5, Erythropoietin (human)
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
 (erythropoietin derivs. for increasing bone marrow production of reticulocytes and erythrocytes)
 RN 11096-26-7 HCAPLUS
 CN Erythropoietin (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

RN 221039-34-5 HCAPLUS
 CN Erythropoietin (human) (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

IT 25322-68-3D, Polyethylene glycol, glycoprotein conjugates
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (erythropoietin derivs. for increasing bone marrow production of reticulocytes and erythrocytes)
 RN 25322-68-3 HCAPLUS
 CN Poly(oxy-1,2-ethanediyl), α -hydro- ω -hydroxy- (9CI) (CA INDEX NAME)



IT 96024-34-9, Erythropoietin (human clone λ HEPOFL13 protein moiety reduced)
 RL: PRP (Properties)
 (unclaimed protein sequence; erythropoietin derivs. for increasing bone marrow production of reticulocytes and erythrocytes)
 RN 96024-34-9 HCAPLUS
 CN Erythropoietin (human clone λ HEPOFL13 protein moiety reduced) (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

L108 ANSWER 17 OF 27 HCAPLUS COPYRIGHT 2005 ACS on STN

AN 2000:435658 HCAPLUS

DN 133:38600

TI The use of subcutaneous **erythropoietin** and intravenous **iron** for the treatment of the anemia of severe, resistant congestive heart failure improves cardiac and renal function and functional cardiac class, and markedly reduces hospitalizations

AU Silverberg, Donald S.; Wexler, Dov; Blum, Miriam; Keren, Gad; Sheps, David; Leibovitch, Eyal; Brosh, David; Laniado, Shlomo; Schwartz, Doron; Yachnin, Tatyana; Shapira, Itzhak; Gavish, Dov; Baruch, Ron; Koifman, Bella; Kaplan, Carl; Steinbruch, Shoshana; Iaina, Adrian

CS Department of Nephrology and Cardiology, Tel Aviv Medical Center, Tel Aviv-Jaffa, Israel

SO Journal of the American College of Cardiology (2000), 35(7), 1737-1744

CODEN: JACCDI; ISSN: 0735-1097

PB Elsevier Science Inc.

DT Journal

LA English

AB This study evaluated the prevalence and severity of anemia in patients with congestive heart failure (CHF) and the effect of its correction on cardiac and renal function and hospitalization. The prevalence and significance of mild anemia in patients with CHF is uncertain, and the role of **erythropoietin** with i.v. **iron** supplementation in treating this anemia is unknown. In a retrospective study, the records of the 142 patients in our CHF clinic were reviewed to find the prevalence and severity of anemia (Hb <12 g). In an intervention study, 26 of these patients, despite maximally tolerated therapy of CHF for at least six months, still had severe CHF and were also anemic. They were treated with s.c. **erythropoietin** and i.v. **iron** sufficient to increase the Hb to 12 g%. The doses of the CHF medications, except for diuretics, were not changed during the intervention period. The prevalence of anemia in the 142 patients increased with the severity of CHF, reaching 79.1% in those with New York Heart Association class IV. In the intervention study, the anemia of the 26 patients was treated for a mean of 7.2±5.5 mo. The mean Hb level and mean left ventricular ejection fraction increased significantly. The mean number of hospitalizations fell by 91.9% compared with a similar period before the study. The New York Heart Association class fell significantly, as did the doses of oral and i.v. furosemide. The rate of fall of the glomerular filtration rate slowed with the treatment. Anemia is very common in CHF and its successful treatment is associated with a significant improvement in cardiac function, functional class, renal function and in a marked fall in the need for diuretics and hospitalization.

IT 7439-89-6, Iron, biological studies

RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)

(use of s.c. **erythropoietin** and i.v. **iron** for treatment of anemia of severe, resistant congestive heart failure improves cardiac and renal function and functional cardiac class, and markedly reduces hospitalizations in humans)

RN 7439-89-6 HCAPLUS

CN Iron (7CI, 8CI, 9CI) (CA INDEX NAME)

Fe

IT 11096-26-7, Erythropoietin

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(use of s.c. erythropoietin and i.v. iron for treatment of anemia of severe, resistant congestive heart failure improves cardiac and renal function and functional cardiac class, and markedly reduces hospitalizations in humans)

RN 11096-26-7 HCAPLUS

CN Erythropoietin (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

RETABLE

Referenced Author (RAU)	Year (RPY)	VOL (RVL)	PG (RPG)	Referenced Work (RWK)	Referenced File
Albitar, S	1998	13	1206	Nephrol Dial Transpl	HCAPLUS
Anand, I	1993	70	357	Br Heart J	MEDLINE
Anand, I	1997	12	251	Curr Opin Cardiol	MEDLINE
Anon	1997	30	193	Am J Kidney Dis	
Anon	1994			Quick reference guid	
Anon	1992	20	32	US Renal Data System	
Besarab, A	1998	339	584	N Engl J Med	HCAPLUS
Carson, J	1995	170	32	Am J Surg	
Carson, J	1996	348	1055	Lancet	MEDLINE
Cline, C	1998	80	442	Heart	MEDLINE
Cowie, M	1997	18	208	Eur Heart J	HCAPLUS
Donnelly, S	1991	14	271	Clin Invest Med	MEDLINE
Elhalel-Dranitzki, M	1998	13	3041	Nephrol Dial Transpl	MEDLINE
Erturk, S	1999	14	1912	Nephrol Dial Transpl	HCAPLUS
Feelders, R	1998	28	520	Eur J Clin Invest	HCAPLUS
Fishbane, S	1995	26	41	Am J Kidney Dis	MEDLINE
Foley, R	1998	9	208	J Am Soc Nephrol	
Fonarow, G	1997	30	725	J Am Coll Cardiol	MEDLINE
Ghali, J	1988	148	2013	Arch Intern Med	MEDLINE
Goch, J	1996	73	403	Nephron	MEDLINE
Goicoechea, M	1998	54	1337	Kidney Intern	HCAPLUS
Goldberg, N	1992	124	424	Am Heart J	MEDLINE
Haber, H	1991	324	353	N Engl J Med	MEDLINE
Herrera-Garza, E	1999	115	1170	Chest	MEDLINE
Hochberg, Y	1974	4	224	J Multivar Anal	
Horl, W	1999	14	50	Nephrol Dial Transpl	
King, D	1996	25	144	Age Ageing	MEDLINE
Koch, K	1995	44	201	Clin Nephrol	HCAPLUS
Kooistra, M	1998	13	828	Nephrol Dial Transpl	
Kuriyama, S	1997	77	176	Nephron	HCAPLUS
Levine, B	1990	323	236	N Engl J Med	MEDLINE
Linde, T	1996	30	115	Scand J Urol Nephrol	MEDLINE
Locatelli, F	1998	13	1642	Nephrol Dial Transpl	MEDLINE
Lopez-Gomez, J	1995	10	31	Nephrol Dial Transpl	
Low, I	1989	31	26	Clin Nephrol	MEDLINE
Low-Friedrich, I	1991	11	54	Am J Nephrol	MEDLINE
Ma, J	1999	10	610	J Am Soc Nephrol	MEDLINE
Macdougall, I	1996	50	1694	Kidney Int	HCAPLUS
Macdougall, I	1998	13	3030	Nephrol Dial Transpl	MEDLINE
Maeda, K	1982	46	137	Jpn Circ J	MEDLINE
Maschio, G	1995	10	74	Nephrol Dial Transpl	
Massie, B	1996	11	221	Curr Opin Cardiol	MEDLINE
Michaelson, A	1998	80	437	Heart	
Opasich, C	1996	78	354	Am J Cardiol	MEDLINE
Packer, M	1999	83	1	Am J Cardiol	

Reis, S	1997	30	733	J Am Coll Cardiol	MEDLINE
Rich, M	1996	44	638	J Am Geriatr Soc	MEDLINE
Rich, M	1995	333	1190	N Engl J Med	MEDLINE
Roth, D	1994	24	777	Am J Kidney Dis	MEDLINE
Scharer, K	1993	82	953	Acta Paediatr	MEDLINE
Schwengel, R	1994	73	908	Am J Cardiol	MEDLINE
Senni, M	1997	72	453	Mayo Clin Proc	MEDLINE
Silagy, C	1993	54	84	Clin Pharmacol Ther	MEDLINE
Silverberg, D	1996	27	234	Am J Kidney Dis	HCAPLUS
Silverberg, D	1999	55	79	Kidney Int	
Silverberg, D	1996	72	413	Nephron	HCAPLUS
Silverberg, D	1998	80	1	Nephron	MEDLINE
Volpe, M	1994	74	468	Am J Cardiol	MEDLINE
Wald, M	1995	71	190	Nephron	HCAPLUS
Weil, J	1995	310	827	Br Med J	MEDLINE
Yoshida, H	1998	53	880	Kidney Int	MEDLINE

L108 ANSWER 18 OF 27 HCAPLUS COPYRIGHT 2005 ACS on STN

AN 1999:573162 HCAPLUS

DN 131:193985

TI The impact of withdrawing ACE inhibitors on **erythropoietin** responsiveness and left ventricular hypertrophy in hemodialysis patients

AU Erturk, Sehsumar; Nergizoglu, Gokhan; Ates, Kenan; Duman, Neval; Erbay, Bulent; Karatan, Oktay; Ertug, A. Ergun

CS Department of Nephrology, Ankara University School of Medicine, Ibn-i Sina Hospital, Ankara, Turk.

SO Nephrology, Dialysis, Transplantation (1999), 14(8), 1912-1916

CODEN: NDTREA; ISSN: 0931-0509

PB Oxford University Press

DT Journal

LA English

AB Background. Angiotensin-converting enzyme (ACE) inhibitors have the capability of decreasing left ventricular mass index (LVMI) in chronic hemodialysis (HD) patients. On the other hand, recent reports provide conflicting information regarding the impact of ACE inhibitors on responsiveness to recombinant human **erythropoietin** (**rHuEpo**), and there are no data about the effect of withdrawing ACE inhibitors both on **rHuEpo** response and LVMI in HD patients. Methods. ACE inhibitors were switched to another antihypertensive medication in 23 out of 68 patients in our HD unit who were receiving both **rHuEpo** and an ACE inhibitor for more than 1 yr. Blood pressure at the pre- and post-dialysis phases, hematocrit levels and **rHuEpo** doses were determined at the end of the first and of the third years, and the LVMI was determined at the end of the third year. Statistical analyses were done in 15 patients in whom the study could be completed. Results. The mean (\pm SD) hematocrit level was increased from $26.3 \pm 6.4\%$ to $29.8 \pm 6.3\%$ at the first year ($P < 0.05$), and to $29.4 \pm 6.5\%$ at the third year ($P < 0.05$ vs. before), while the mean dose of **rHuEpo** was decreased from 208.3 ± 99.0 UI/kg/wk to 141.0 ± 91.8 at the first year ($P = 0.01$), and to 141.4 ± 81.0 at the third year ($P = 0.01$ vs. before). Administration of **rHuEpo** had been stopped in two patients at the end of the first year. The mean blood pressure level and the mean LVMI were not changed ($P > 0.05$ vs. before). There were no significant changes in dialysis parameters, iron status, plasma renin activities, and levels of aldosterone, intact parathyroid hormone, aluminum and **erythropoietin**. Conclusion. The findings of this small uncontrolled study indicate that withdrawal of ACE inhibitors in hypertensive chronic HD patients receiving **rHuEpo** may result in an increase in hematocrit level, and a decrease in dose of **rHuEpo** without any significant changes in the blood pressure level and LVMI.

Controlled prospective studies are needed to clarify this issue.

IT 11096-26-7, **Erythropoietin**

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(impact of withdrawing ACE inhibitors on **erythropoietin** responsiveness and left ventricular hypertrophy in humans on hemodialysis)

RN 11096-26-7 HCAPLUS

CN Erythropoietin (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

RETABLE

Referenced Author (RAU)	Year (RPY)	VOL (RVL)	PG (RPG)	Referenced Work (RWK)	Referenced File
Akpolat, T	1998	11	94	J Nephrol	MEDLINE
Albitar, S	1998	13	1206	Nephrol Dial Transpl	HCAPLUS
Bauer, J	1996		2331	The Kidney	
Cannella, G	1997	30	659	Am J Kidney Dis	HCAPLUS
Conlon, P	1994	9	1358	Nephrol Dial Transpl	MEDLINE
Constantinescu, C	1998	62	25	Immunol Lett	HCAPLUS
Cruz, D	1996	28	535	Am J Kidney Dis	HCAPLUS
Daugirdas, J	1993	4	1205	J Am Soc Nephrol	MEDLINE
Devereux, R	1986	57	450	Am J Cardiol	MEDLINE
Diez, J	1994	12	S31	J Hypertens	
Dyadyk, A	1997	12	945	Nephrol Dial Transpl	HCAPLUS
Erturk, S	1996	11	2050	Nephrol Dial Transpl	MEDLINE
Erturk, S	1996	11	396	Nephrol Dial Transpl	MEDLINE
Escbach, J	1988	11	203	Am J Kidney Dis	
Escbach, J	1997	30	S192	Am J Kidney Dis	
Goicoechea, M	1998	54	1337	Kidney Int	HCAPLUS
Gossmann, J	1996	50	973	Kidney Int	HCAPLUS
Gould, A	1990	181	225	Eur J Pharmacol	HCAPLUS
Gould, A	1980	96	523	J Lab Clin Med	HCAPLUS
Greaves, S	1994	24	768	Am J Kidney Dis	MEDLINE
Hirakata, H	1986	26	27	Clin Nephrol	MEDLINE
Julian, B	1998	9	1104	J Am Soc Nephrol	HCAPLUS
Kamper, A	1990	50	611	Scand J Clin Lab Inv	MEDLINE
Macdougall, I	1994	9	1032	Nephrol Dial Transpl	
Macdougall, I	1998	13	23	Nephrol Dial Transpl	
Morrone, L	1997	64	913	Transplantation	HCAPLUS
Motz, W	1987	10	S148	J Cardiovasc Pharmac	
Mrug, M	1997	100	2310	J Clin Invest	HCAPLUS
Naeshiro, I	1998	354	179	Eur J Pharmacol	HCAPLUS
Nakao, K	1967	29	754	Blood	HCAPLUS
Navarro, J	1998	80	239	Nephron	MEDLINE
Sahn, D	1978	58	1072	Circulation	MEDLINE
Sasaki, M	1996	12	1403	J Hypertens	
Schwenk, M	1998	18	627	Pharmacotherapy	HCAPLUS
Sennesael, J	1985	28	A252	Kidney Int	
Silberberg, J	1989	64	222	Am J Cardiol	MEDLINE
Silberberg, J	1990	6	1	Can J Cardiol	MEDLINE
Sundal, E	1991	6	955	Nephrol Dial Transpl	MEDLINE

L108 ANSWER 19 OF 27 HCAPLUS COPYRIGHT 2005 ACS on STN

AN 1999:280686 HCAPLUS

DN 130:332154

TI Is there a role for adjuvant therapy in patients being treated with epoetin?

AU Horl, W. H.
 CS Department of Nephrology, University of Vienna, Vienna, Austria
 SO Nephrology, Dialysis, Transplantation (1999), 14(Suppl. 2),
 50-60
 CODEN: NDTREA; ISSN: 0931-0509
 PB Oxford University Press
 DT Journal; General Review
 LA English
 AB A review with 78 refs. Adjuvant therapy may allow patients being treated with **epoetin** to derive greater clin. benefits. **Iron** supplementation is currently the most widely used form of adjuvant therapy; i.v. (i.v.) **iron** is required by the majority of haemodialysis patients receiving **epoetin**. Measurement of hypochromic red blood cells is the most direct way of assessing **iron** supply to the bone marrow. During the correction phase, a dose of i.v. **iron** equivalent to 50 mg/day is recommended, with the total dose not exceeding 3 g. When subclin. vitamin C deficiency is suspected, ascorbic acid may be given orally (1-1.5 g/wk) or i.v. (300 mg three times weekly at the end of dialysis). The active vitamin D metabolites alfacalcidol and calcitriol may, under some circumstances, improve anemia and reduce **epoetin** dosage requirements. Vitamin B6 requirements are increased during **epoetin** therapy, and supplementation at a dose of 100-150 mg/wk is recommended. Supplementation of vitamin B12 is optional. Folic acid is supplemented routinely in haemodialysis patients, though evidence that it increases the efficacy of **epoetin** is limited. Low doses (2-3 mg/wk) should normally be sufficient to maintain optimal folic acid stores in **epoetin**-treated patients, although higher doses are necessary for patients with hyperhomocysteinemia. L-Carnitine supplementation may be appropriate in some patients with anemia of chronic renal failure (CRF) unresponsive to, or requiring large doses of, **epoetin**. Androgens potentially could reduce **epoetin** costs in countries with limited resources, but should only be used in men older than 50 yr with a remnant kidney. Recent animal studies indicate that the combination of **epoetin** and insulin-like growth factor 1 might be beneficial in CRF patients. High doses of angiotensin-converting enzyme (ACE) inhibitors should be reserved for dialysis patients who have hypertension that cannot be controlled by other agents, or who require an ACE inhibitor for treatment of heart failure.

IT 7439-89-6, **Iron**, biological studies 11096-26-7
 , **Epoetin**
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (epoetin and adjuvant therapy in humans)

RN 7439-89-6 HCAPLUS
 CN Iron (7CI, 8CI, 9CI) (CA INDEX NAME)

Fe

RN 11096-26-7 HCAPLUS
 CN Erythropoietin (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

RETABLE

Referenced Author (RAU)	Year (RPY)	VOL (RVL)	PG (RPG)	Referenced Work (RWK)	Referenced File
Albitar, S	1994	9	1027	Nephrol Dial Transpl	
Albitar, S	1997	12	514	Nephrol Dial Transpl	HCAPLUS

Albitar, S	1997	12	514	Nephrol Dial Transpl	HCAPLUS
Albitar, S	1998	13	1206	Nephrol Dial Transpl	HCAPLUS
Argiles, A	1994	9	1809	Nephrol Dial Transpl	MEDLINE
Argiles, A	1994	9	1809	Nephrol Dial Transpl	MEDLINE
Azizi, M	1996	97	839	J Clin Invest	HCAPLUS
Ballal, S	1991	17	29	Am J Kidney Dis	MEDLINE
Barany, P	1997	29	565	Am J Kidney Dis	HCAPLUS
Barbour, G	1979	139	889	Arch Intern Med	MEDLINE
Berard, E	1992	62	368	Nephron	MEDLINE
Berns, J	1992	37	264	Clin Nephrol	MEDLINE
Boran, M	1996	73	314	Nephron	MEDLINE
Brox, A	1996	50	937	Kidney Int	HCAPLUS
Brox, A	1998	66	1053	Transplantation	HCAPLUS
Carozzi, S	1990	6	312	Adv Peritoneal Dial	MEDLINE
Carozzi, S	1997	43	M535	J Am Soc Artif Inter	MEDLINE
Christ, E	1997	82	2985	J Clin Endocrinol Me	HCAPLUS
Conlon, P	1994	9	1358	Nephrol Dial Transpl	MEDLINE
Consensus Group Stateme	1994	23	177	Dial Transplant	
Cruz, D	1996	28	535	Am J Kidney Dis	HCAPLUS
Descombes, E	1993	43	1319	Kidney Int	MEDLINE
Eder, M	1997	15	327	Stem Cells	HCAPLUS
Fishbane, S	1995	26	41	Am J Kidney Dis	MEDLINE
Gastaldello, K	1995	10	44	Nephrol Dial Transpl	
Gaughan, K	1997	30	495	Am J Kidney Dis	
Gobel, V	1994	153	43	Eur J Pediatr	MEDLINE
Goicoechea, M	1998	78	23	Nephron	HCAPLUS
Gokal, R	1979	48	393	Q J Med	MEDLINE
Golper, T	1992	5	94	Semin Dial	
Hampers, C	1967	276	551	N Engl J Med	MEDLINE
Hess, E	1996	11	749	Nephrol Dial Transpl	MEDLINE
Hunter, R	1970	1	61	Lancet	MEDLINE
Hutchison, F	1997	29	651	Am J Kidney Dis	
Julian, B	1994	46	1397	Kidney Int	MEDLINE
Kamper, A	1990	50	611	Scand J Clin Lab Inv	MEDLINE
Kasama, R	1996	27	680	Am J Kidney Dis	MEDLINE
Kooistra, M	1991	57	127	Nephron	MEDLINE
Kurtz, A	1990	122	323	Acta Endocrinol	HCAPLUS
Kurtz, A	1982	149	105	FEBS Lett	HCAPLUS
Kurtz, A	1988	85	7825	Proc Natl Acad Sci U	HCAPLUS
Labonia, W	1995	26	757	Am J Kidney Dis	HCAPLUS
Labonia, W	1987	32	754	Kidney Int	HCAPLUS
Lederle, R	1990	105	1307	Dtsch Med Wochenschr	
Macdougall, I	1989	299	157	Br Med J	MEDLINE
Macdougall, I	1992	304	225	Br Med J	MEDLINE
Macdougall, I	1996	50	1694	Kidney Int	HCAPLUS
Macdougall, I	1995	10	607	Nephrol Dial Transpl	MEDLINE
Matsumura, M	1996	72	574	Nephron	MEDLINE
Matsumura, M	1997	77	164	Nephron	HCAPLUS
Matsuzaki, Y	1996	63	33	Int J Hematol	MEDLINE
Moore, L	1992	3	105	J Renal Nutr	
Morrone, L	1997	64	913	Transplantation	HCAPLUS
Muta, K	1993	156	264	J Cell Physiol	HCAPLUS
Mydlik, M	1997	51	S56	Kidney Int	
Ono, K	1992	38	290	Clin Nephrol	MEDLINE
Pronai, W	1995	71	395	Nephron	HCAPLUS
Rao, D	1993	328	171	N Engl J Med	MEDLINE
Rolton, H	1991	6	440	Nephrol Dial Transpl	MEDLINE
Sanchez, J	1995	10	1476	Nephrol Dial Transpl	MEDLINE
Shimizu, T	1994	47	178	Am J Hematol	MEDLINE
Sunder-Plassmann, G	1995	10	2070	Nephrol Dial Transpl	MEDLINE

Taniguchi, S	1997	90	2244	Blood	HCAPLUS
Tarnng, D	1998	9	227A	J Am Soc Nephrol	
Tarnng, D	1998	13	2867	Nephrol Dial Transpl	HCAPLUS
Tarnng, D	1997	3	S189	Nephrology	
Teruel, J	1996	7	140	J Am Soc Nephrol	HCAPLUS
Teruel, J	1996	30	129	Scand J Urol Nephrol	MEDLINE
Teruel, J	1996	30	403	Scand J Urol Nephrol	HCAPLUS
Tinawi, M	1996	74	291	Nephron	MEDLINE
Urena, P	1992	7	40	Nephrol Dial Transpl	MEDLINE
Urena, P	1991	59	384	Nephron	MEDLINE
Vihervuori, E	1996	87	2075	Blood	HCAPLUS
Vlahakos, D	1991	17	199	Am J Kidney Dis	MEDLINE
Vlahakos, D	1995	43	53	Clin Nephrol	MEDLINE
Walter, J	1993	8	1428	Nephrol Dial Transpl	MEDLINE
Westwood, N	1994	86	468	Br J Haematol	HCAPLUS
Zachee, P	1992	12	188	Am J Nephrol	MEDLINE

L108 ANSWER 20 OF 27 HCAPLUS COPYRIGHT 2005 ACS on STN

AN 1998:588841 HCAPLUS

DN 130:762

TI The effects of normal as compared with low hematocrit values in patients with cardiac disease who are receiving hemodialysis and **epoetin**

AU Besarab, Anatole; Bolton, Kline; Browne, Jeffrey K.; Egrie, Joan C.; Nissenson, Allen R.; Okamoto, Douglas M.; Schwab, Steve J.; Goodkin, David A.

CS Division of Nephrology and Hypertension, Henry Ford Hospital, Detroit, USA

SO New England Journal of Medicine (1998), 339(9), 584-590

CODEN: NEJMAG; ISSN: 0028-4793

PB Massachusetts Medical Society

DT Journal

LA English

AB In patients with end-stage renal disease, anemia develops as a result of **erythropoietin** deficiency, and recombinant human **erythropoietin (epoetin)** is prescribed to correct the anemia partially. We examined the risks and benefits of normalizing the hematocrit in patients with cardiac disease who were undergoing hemodialysis. We studied 1233 patients with clin. evidence of congestive heart failure or ischemic heart disease who were undergoing hemodialysis: 618 patients were assigned to receive increasing doses of **epoetin** to achieve and maintain a hematocrit of 42 percent, and 615 were assigned to receive doses of **epoetin** sufficient to maintain a hematocrit of 30 percent throughout the study. The median duration of treatment was 14 mo. The primary end point was the length of time to death or a first nonfatal myocardial infarction. After 29 mo, there were 183 deaths and 19 first nonfatal myocardial infarctions among the patients in the normal-hematocrit group and 150 deaths and 14 nonfatal myocardial infarctions among those in the low-hematocrit group (risk ratio for the normal-hematocrit group as compared with the low hematocrit group, 1.3; 95 percent confidence interval, 0.9 to 1.9). Although the difference in event-free survival between the two groups did not reach the prespecified statistical stopping boundary, the study was halted. The causes of death in the two groups were similar. The mortality rates decreased with increasing hematocrit values in both groups. The patients in the normal-hematocrit group had a decline in the adequacy of dialysis and received i.v. iron dextran more often than those in the low-hematocrit group. In patients with clin. evident congestive heart failure or ischemic heart disease who are receiving hemodialysis, administration of **epoetin** to raise their hematocrit to 42 percent is not recommended.

IT 11096-26-7, Epoetin

RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (effects of normal as compared with low hematocrit values in humans with cardiac disease who are receiving hemodialysis and epoetin
)

RN 11096-26-7 HCAPLUS

CN Erythropoietin (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

RETABLE

Referenced Author (RAU)	Year (RPY)	VOL (RVL)	PG (RPG)	Referenced Work (RWK)	Referenced File
Barany, P	1996	7	1472	J Am Soc Nephrol abs	
Benz, R	1996	7	1473	J Am Soc Nephrol abs	
Beusterien, K	1996	7	763	J Am Soc Nephrol	HCAPLUS
Braumann, K	1991	58	129	Nephron	MEDLINE
Canadian Erythropoietin	1990	300	573	BMJ	
Cannella, G	1991	6	31	Nephrol Dial Transpl	MEDLINE
Collins, A	1994	5	439	J Am Soc Nephrol abs	
Collins, A	1997	8	190A	J Am Soc Nephrol abs	
Cox, D	1972	34	187	J R Stat Soc [B]	
Eschbach, J	1989	111	992	Ann Intern Med	MEDLINE
Eschbach, J	1993	4	425	J Am Soc Nephrol abs	
Eschbach, J	1993	6	180	Semin Dial	
Evans, R	1990	263	825	JAMA	MEDLINE
Goldberg, N	1992	124	424	Am Heart J	MEDLINE
Hoen, B	1995	10	377	Nephrol Dial Transpl	MEDLINE
Jennison, C	1990	5	299	Stat Sci	
Kusunoki, M	1981	1	413	J Cereb Blood Flow M	MEDLINE
Lan, K	1983	70	659	Biometrika	
Lowrie, E	1995			The anemia of ESRD a	
Lundin, A	1991	58	315	Nephron	MEDLINE
Macdougall, I	1990	335	614	Erratum Lancet	
Macdougall, I	1990	335	489	Lancet	MEDLINE
Marsh, J	1991	39	155	Kidney Int	MEDLINE
Massachusetts General H	1992	327	718	N Engl J Med	
McHorney, C	1993	31	247	Med Care	MEDLINE
Muirhead, N	1993	6	184	Semin Dial	
National Institute Of D	1996		23	Renal Data System US	
Nissenson, A	1996	7	1459	J Am Soc Nephrol abs	
Parfrey, P	1990	10	213	Am J Nephrol	MEDLINE
Parfrey, P	1991	2	2	J Am Soc Nephrol	MEDLINE
Pascual, J	1991	35	280	Clin Nephrol	MEDLINE
Rostand, S	1990		409	Clinical dialysis 2n	
Salonen, J	1992	86	803	Circulation	HCAPLUS
Sennesael, J	1991	40	121	Kidney Int	MEDLINE
Silberberg, J	1989	36	286	Kidney Int	MEDLINE
Sullivan, J	1981	1	1293	Lancet	HCAPLUS
Tielemans, C	1989	4	883	Nephrol Dial Transpl	MEDLINE
Veys, N	1992	19	358	Am J Kidney Dis	MEDLINE
Wizemann, V	1992	62	161	Nephron	MEDLINE
Zehnder, C	1992	61	21	Nephron	MEDLINE

L108 ANSWER 21 OF 27 HCAPLUS COPYRIGHT 2005 ACS on STN

AN 1998:329025 HCAPLUS

DN 129:67164

TI The estimation of efficacy of oral iron supplementation during treatment with epoetin beta (recombinant human

erythropoietin) in patients undergoing cardiac surgery

AU Sowade, Olaf; Messinger, Diethelm; Franke, Werner; Sowade, Birgit;
CS Scigalla, Paul; Warnke, Harry
Department of Cardiac Surgery, Charite-Hospital, Humboldt University
Berlin, Mannheim, Germany
SO European Journal of Haematology (1998), 60(4), 252-259
CODEN: EJHAEC; ISSN: 0902-4441
PB Munksgaard International Publishers Ltd.
DT Journal
LA English
AB We estimated the efficacy of oral iron therapy during treatment with
rhEPO (**erythropoietin**) in patients undergoing cardiac surgery
who were contraindicated for autologous blood donation. Seventy-six
patients were enrolled in this double-blind, placebo-controlled trial and
assigned to the 2 treatment groups (5+500 U/kg body weight rhEPO or
placebo i.v. over 14 d before surgery). During the treatment period all
patients received 300 mg Fe2+ (**iron glycine sulfate**) orally per
day. RhEPO therapy produced significant increases in Hb concentration (Hb),
reticulocyte count, hematocrit (Hct) and the hypochromic red blood cells
(HRBC), and a decrease in transferrin saturation (41%) compared to the placebo
group before surgery. However, the preoperative increase in HRBC was
independent of the baseline ferritin and even correlated pos. with the
preoperative increase in Hct ($r=0.47$, $p<0.01$). In rhEPO patients there
were inverse correlations between baseline serum iron and the
preoperative increases in Hb ($r=-0.39$, $p<0.05$), Hct ($r=-0.50$, $p<0.01$) and
HRBC ($r=-0.53$, $p<0.001$). With this treatment regimen the HRBC appear to
reflect the degree of erythropoietic stimulation rather than functional
iron deficiency. The preoperative increases in reticulocytes,
HRBC and Hb/Hct in patients with ferritin <100 mg/l or transferrin saturation
<16% showed no significant difference compared to their complementary
groups. The preoperative decrease in storage iron and the
inverse correlation between the baseline ferritin and the preoperative
change in ferritin ($r=-0.94$, $p<0.0001$) in the rhEPO group indicate that
the iron requirement for Hb synthesis is probably covered by the
breakdown of stored iron and an increase in the rate of
absorption of orally administered Fe2+. I.v. rhEPO treatment with
5+500 U/kg body weight in combination with 300 mg oral Fe2+/d given
over 14 d before surgery is a suitable regimen to increase Hb by about
1.61 g/dL and Hct by 0.06.

IT 7439-89-6, Iron, biological studies
RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)
(deficiency; estimation of efficacy of oral iron supplementation
during treatment with **epoetin beta** (recombinant
human **erythropoietin**) in patients undergoing cardiac surgery)

RN 7439-89-6 HCAPLUS
CN Iron (7CI, 8CI, 9CI) (CA INDEX NAME)

Fe

IT 7439-89-6D, Iron, glycine sulfate complexes, biological
studies
RL: BAC (Biological activity or effector, except adverse); BSU (Biological
study, unclassified); BIOL (Biological study)
(estimation of efficacy of oral iron supplementation during
treatment with **epoetin beta** (recombinant human
erythropoietin) in patients undergoing cardiac surgery)

RN 7439-89-6 HCAPLUS
CN Iron (7CI, 8CI, 9CI) (CA INDEX NAME)

Fe

IT 11096-26-7, **Erythropoietin**

RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)

(rhEPO; estimation of efficacy of oral iron supplementation during treatment with **epoetin beta** (recombinant human **erythropoietin**) in patients undergoing cardiac surgery)

RN 11096-26-7 HCAPLUS

CN Erythropoietin (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

RETABLE

Referenced Author (RAU)	Year (RPY)	VOL (RVL)	PG (RPG)	Referenced Work (RWK)	Referenced File
Adamson, J	1993		161	Erythropoietin - mol	HCAPLUS
Beguin, Y	1997	90	A36	Blood	
Biesma, D	1994	86	30	Br J Haematol	MEDLINE
Brugnara, C	1993	81	956	Blood	MEDLINE
Brugnara, C	1994	123	660	J Lab Clin Med	HCAPLUS
Brunner, W	1995	5	122	J Suisse Pharm	
Canadian Orthopedic Per	1993	341	1227	Lancet	
Cavill, I	1975	256	328	Nature	HCAPLUS
Cazzola, M	1997	89	4248	Blood	HCAPLUS
Cook, J	1990	51	301	Am J Clin Nutr	HCAPLUS
Cook, J	1986	68	726	Blood	MEDLINE
Cook, J	1990	75	603	Br J Haematol	MEDLINE
Donohue, D	1958	37	1564	J Clin Invest	MEDLINE
Eschbach, J	1991	88	72	Contrib Nephrol	MEDLINE
Eschbach, J	1987	316	73	N Engl J Med	MEDLINE
Finch, C	1982	60	1241	Blood	HCAPLUS
Goodnough, L	1991	188	289	J Lab Clin Med	
Goodnough, L	1989	321	1163	N Engl J Med	MEDLINE
Horl, W	1996	11	246	Nephrol Dial Transpl	MEDLINE
Kumpf, V	1990	24	162	Ann Pharmacother	MEDLINE
Macdougall, I	1992	304	225	Br Med J	MEDLINE
Mercuriali, F	1995	6	67	Erythropoiesis	
Mercuriali, F	1993	33	55	Transfusion	MEDLINE
Meyer, M	1996	129	258	J Pediatr	HCAPLUS
Nadler, S	1962	51	224	Surgery	
Price, T	1996	36	29	Transfusion	MEDLINE
Silverberg, D	1996	72	413	Nephron	HCAPLUS
Skikne, B	1990	75	1870	Blood	HCAPLUS
Skikne, B	1993		177	Erythropoietin - mol	HCAPLUS
Skikne, B	1992	120	746	J Lab Clin Med	HCAPLUS
Sowade, O	1997	55	89	Am J Hematol	HCAPLUS
Sowade, O	1997	89	411	Blood	HCAPLUS
Sowade, O	1997	129	97	J Lab Clin Med	HCAPLUS

L108 ANSWER 22 OF 27 HCAPLUS COPYRIGHT 2005 ACS on STN

AN 1998:88081 HCAPLUS

DN 128:124107

TI Evaluation of erythropoietic activity on the basis of the red cell and reticulocyte distribution widths during **epoetin beta** therapy in patients undergoing cardiac surgery

AU Sowade, Olaf; Sowade, Birgit; Gross, Johann; Brilla, Kay; Ziemer, Sabine;
Franke, Werner; Stephan, Peter; Scigalla, Paul; Warnke, Harry
CS Dep. Heart Surgery, Medical Fac.; Humboldt Univ., Berlin, Germany
SO Acta Haematologica (1998), 99(1), 1-7
CODEN: ACHAAH; ISSN: 0001-5792
PB S. Karger AG
DT Journal
LA English
AB The changes in the red cell and reticulocyte distribution widths during
preoperative treatment with recombinant human **erythropoietin**
(rhEPO) were evaluated in a double-blind, placebo-controlled trial in
cardiac surgery patients. The increases in the reticulocyte count, in the
Hb and in all distribution widths are the expression of the marked
preoperative stimulation of erythropoiesis in the patients treated with
rhEPO. Only placebo patients with a Hb ≤ 7.5 mmol/l or a
transferrin > 4.0 g/l at baseline showed an increase in the red cell
distribution width or in the reticulocyte Hb distribution width on oral
iron therapy alone. While the reticulocyte count and the
distribution widths of red cells in the rhEPO patients decreased
postoperatively, only the increases in the distribution widths of
reticulocytes after the second postoperative day indicate that stimulation
of erythropoiesis had taken place. In patients with a low Hb or a high
transferrin the rhEPO therapy should be preceded by **iron** therapy
in order to raise the Hb level and reduce the cost of treatment.

IT 122312-54-3, **Epoetin beta**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological
study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES
(Uses)
(evaluation of erythropoietic activity on the basis of the red cell and
reticulocyte distribution widths during **epoetin beta**
therapy in patients undergoing cardiac surgery)

RN 122312-54-3 HCAPLUS
CN 1-165-Erythropoietin (human clone λ HEPOFL13 protein moiety),
glycoform β (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

L108 ANSWER 23 OF 27 HCAPLUS COPYRIGHT 2005 ACS on STN
AN 1997:466755 HCAPLUS
DN 127:131546
TI Kinetics of reticulocyte maturity fractions and indices and **iron**
status during therapy with **epoetin beta** (recombinant
human **erythropoietin**) in cardiac surgery patients
AU Sowade, Olaf; Sowade, Birgit; Brilla, Kay; Franke, Werner; Stephan, Peter;
Gross, Johann; Scigalla, Paul; Warnke, Harry
CS Cardiac Surgery Clinic, Medical Faculty (Charite), Humboldt University,
Berlin, Germany
SO American Journal of Hematology (1997), 55(2), 89-96
CODEN: AJHEDD; ISSN: 0361-8609
PB Wiley-Liss
DT Journal
LA English
AB We evaluated the changes in reticulocyte maturity fractions and indexes,
as measured by flow cytometry, during preoperative treatment with
recombinant human **erythropoietin** (**epoetin beta**
) in cardiac surgery patients. A total of 72 patients was enrolled in
this double-blind, randomized, placebo-controlled clin. trial and assigned
to the two treatment groups (5 + 500 U/kg bodyweight **epoetin**
beta or placebo i.v. over 14 days preoperatively). Therapy with
epoetin beta produced continuous increases in

hematocrit/Hb, in the most mature fraction of reticulocytes (LR), and in reticulocyte count. In the first treatment week there were parallel increases in the fraction of most immature reticulocytes (HR) and in the reticulocyte mean cell volume. During the second week of treatment the reticulocyte mean cell Hb content (CHr) decreased, but CHr was independent of all iron parameters, affecting neither the reticulocyte fractions nor the hematocrit/Hb increase. The total preoperative rise in hematocrit correlated with the rises in LR fraction ($P = 0.0270$) and reticulocyte count ($P = 0.0486$) during the first week of treatment. Whereas in the **epoetin beta** patients the preoperative change in HR fraction showed neg. correlations with transferrin saturation at baseline ($P = 0.0058$) and with the preoperative change in iron ($P = 0.0113$), the preoperative change in the LR fraction correlated pos. with transferrin at baseline ($P = 0.0115$). Postoperatively, the reticulocyte parameters revealed that the onset of increased stimulation of erythropoiesis did not occur in the placebo patients until the second postoperative day, whereas erythropoietic activity in the **epoetin beta** patients was much higher during the postoperative period as well, as a result of the preoperative stimulation of erythropoiesis. The reticulocyte parameters measured by flow cytometry permitted an objective anal. of erythropoietic activity during treatment with **epoetin beta** and in all patients post-operatively. Further studies in various types of **epoetin beta** therapy are needed in order to clarify the value of these reticulocyte parameters for identification of iron deficiency and optimization of **epoetin beta** treatment regimen.

IT 7439-89-6, Iron, biological studies

RL: BOC (Biological occurrence); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence); PROC (Process)

(kinetics of reticulocyte maturity fractions and indexes and iron status during therapy with **epoetin beta** in cardiac surgery patients)

RN 7439-89-6 HCAPLUS

CN Iron (7CI, 8CI, 9CI) (CA INDEX NAME)

Fe

IT 122312-54-3, **Epoetin beta**

RL: BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)

(kinetics of reticulocyte maturity fractions and indexes and iron status during therapy with **epoetin beta** in cardiac surgery patients)

RN 122312-54-3 HCAPLUS

CN 1-165-Erythropoietin (human clone λ HEPOFL13 protein moiety), glycoform β (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

RETABLE

Referenced Author (RAU)	Year (RPY)	VOL (RVL)	PG (RPG)	Referenced Work (RWK)	Referenced File
Adamson, J	1968	44	725	Am J Med	MEDLINE
Bidstrup, B	1993	55	971	Ann Thorac Surg	MEDLINE
Brugnara, C	1994	102	623	Am J Clin Pathol	MEDLINE
Brugnara, C	1994	123	660	J Lab Clin Med	HCAPLUS
Eschbach, J	1987	316	73	N Engl J Med	MEDLINE

Ganzoni, A	1969	16	119	Br J Haematol	MEDLINE
Goodnough, L	1989	321	1163	N Engl J Med	MEDLINE
Kampf, D	1989	76	106	Contrib Nephrol	MEDLINE
Labardini, J	1973	7	301	Haematology	HCAPLUS
Lee, L	1986	7	508	Cytometry	HCAPLUS
Levine, E	1989	106	432	Surgery	MEDLINE
Lowenstein, L	1959	8	135	Int Rev Cytol	HCAPLUS
Rapoport, S	1986		1	The Reticulocyte	
Schmoeckel, M	1993	41	364	Thorac Cardiovasc Su	MEDLINE
Sowade, O	1995	44	257	Anaesthesist	MEDLINE
Sowade, O	1997	89	411	Blood	HCAPLUS
Sowade, O	1995	33	37a	Eur J Clin Chem Clin	
Tatsumi, N	1990	82	41	Contrib Nephrol	MEDLINE
Wells, D	1992	97	130	Am J Clin Pathol	MEDLINE
Yataganas, X	1970	62	254	Exp Cell Res	MEDLINE

L108 ANSWER 24 OF 27 HCAPLUS COPYRIGHT 2005 ACS on STN

AN 1997:51720 HCAPLUS

DN 126:127308

TI Avoidance of allogeneic blood transfusions by treatment with
epoetin beta (recombinant human **erythropoietin**
) in patients undergoing open-heart surgery

AU Sowade, Olaf; Warnke, Harry; Scigalla, Paul; Sowade, Birgit; Franke,
Werner; Messinger, Diethelm; Gross, Johann

CS Med. Fac., Humboldt Univ., Berlin, Germany

SO Blood (1997), 89(2), 411-418

CODEN: BLOOAW; ISSN: 0006-4971

PB Saunders

DT Journal

LA English

AB In a double-blind, randomized, placebo-controlled trial, we evaluated the ability of **epoetin beta** (recombinant human **erythropoietin**) to avoid allogeneic blood transfusions (ABT) and the associated risks in patients undergoing primary elective open-heart surgery and in whom autologous blood donation (ABD) was contraindicated. Seventy-six patients overall were enrolled onto the trial and were randomly assigned to the two treatment groups, 5+500 U/kg body weight (BW) **epoetin beta** or placebo i.v. over 14 days preoperatively. All patients received 300 mg Fe²⁺ orally per day during the treatment period. Preoperatively, the mean Hb increase was 1.50 g/dL greater in **epoetin beta** patients than in placebo patients (95% confidence interval, 1.10 to 1.90 g/dL), allowing a rapid return to the baseline value by the seventh postoperative day in most **epoetin beta** patients. The mean volume of blood collected by intraoperative isovolemic hemodiln. was 562 mL (red blood cell mass, 274 mL) in the **epoetin beta** group and 218 mL (red blood cell mass, 94 mL) in the placebo group, resp. Only four patients (11%) in the **epoetin beta** group received an ABT, compared with 19 (53%) in the placebo group. **Epoetin beta** was most useful in patients with a perioperative blood loss greater than 750 mL, in those with a baseline hematocrit value less than 0.42, and in those aged ≥60 yr. The iron supplementation proved adequate despite the fact that a significant decrease in ferritin (median, 48.1%) and transferrin saturation (median, 40.5%) was observed in **epoetin beta** patients preoperatively. No influence of **epoetin beta** therapy on blood pressure, laboratory safety variables, or the frequency of specific adverse events was observed. I.v. **epoetin beta** treatment of 5+500 U/kg BW in combination with 300 mg Fe²⁺ orally per day administered over 14 days preoperatively is an adequate therapy for increasing mean Hb levels by

approx. 1.50 g/dL and reducing the allogeneic blood requirement in patients undergoing elective open-heart surgery and in whom ABD is contraindicated.

IT 7439-89-6, Iron, biological studies 122312-54-3
, Epoetin beta

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(avoidance of allogeneic blood transfusions by treatment with epoetin beta (recombinant human erythropoietin) in combination with iron in patients undergoing open-heart surgery)

RN 7439-89-6 HCAPLUS

CN Iron (7CI, 8CI, 9CI) (CA INDEX NAME)

Fe

RN 122312-54-3 HCAPLUS

CN 1-165-Erythropoietin (human clone λ HEPOFL13 protein moiety), glycoform β (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

RETABLE

Referenced Author (RAU)	Year (RPY)	VOL (RVL)	PG (RPG)	Referenced Work (RWK)	Referenced File
Bidstrup, B	1993	55	971	Ann Thorac Surg	MEDLINE
Biesma, D	1994	344	367	Lancet	MEDLINE
Bommer, J	1988	2	406	Lancet	MEDLINE
Brugnara, C	1994	123	660	J Lab Clin Med	HCAPLUS
Canadian Orthopedic Per	1993	341	1227	Lancet	
Casagrande, J	1978	34	483	Biometrics	MEDLINE
Cosgrove, D	1985	40	380	Ann Thorac Surg	MEDLINE
Duke, M	1969	39	503	Circulation	MEDLINE
Eschbach, J	1987	316	73	N Engl J Med	MEDLINE
Geraci, J	1993	118	18	Ann Intern Med	MEDLINE
Goodnough, L	1995	60	473	Ann Thorac Surg	MEDLINE
Goodnough, L	1991	266	86	JAMA	
Goodnough, L	1989	321	1163	N Engl J Med	MEDLINE
Hammermeister, K	1990	82	IV-380	Circulation	
Hollander, M	1973			Nonparametric Statis	
Knight, A	1988	68	681	Anesthesiology	MEDLINE
Kyo, S	1992	86	II-413	Circulation	
Kyo, S	1992	86	II-17	Circulation abstr 28	
Levine, E	1989	106	432	Surgery	MEDLINE
Lewis, C	1991	51	448	Ann Thorac Surg	MEDLINE
McDougall, I	1989	299	157	Br Med J	
McMahon, F	1990	76	1718	Blood	HCAPLUS
Nadler, S	1962	51	224	Surgery	
Price, T	1996	36	29	Transfusion	MEDLINE
Robertie, P	1990	28	197	Int Anaesthesiol Cli	MEDLINE
Rutherford, C	1994	96	139	Am J Med	MEDLINE
Schmoeckel, M	1993	41	364	Thorac Cardiovasc Su	MEDLINE
Schooley, J	1987	67	11	Br J Haematol	HCAPLUS
Scott, W	1992	103	1001	J Thorac Cardiovasc	MEDLINE
Skikne, B	1992	120	746	J Lab Clin Med	HCAPLUS
Sowade, O	1995	44	257	Anaesthesist	MEDLINE
Sowade, O	1995	86	352a	Blood	

Welch, H | 1992 | 116 | 393 | Ann Intern Med | MEDLINE

L108 ANSWER 25 OF 27 HCAPLUS COPYRIGHT 2005 ACS on STN

AN 1996:309221 HCAPLUS

DN 125:2127

TI Perioperative **epoetin alfa** reduces transfusion requirements in coronary artery bypass graft surgery

AU D'Ambra, Michael

CS Massachusetts General Hospital, Boston, MA, 02114, USA

SO Seminars in Hematology (1996), 33(2, Suppl. 2), 73-74

CODEN: SEHEA3; ISSN: 0037-1963

PB Saunders

DT Journal

LA English

AB Patients undergoing cardiac surgery continue to be exposed to allogeneic blood. **Epoetin alfa** has been shown to reduce allogeneic blood requirements in patients scheduled for cardiac surgery, principally by facilitating autologous blood (AB) predonation. However, for some patients, there may not be sufficient time to donate AB prior to surgery. In this group of patients, the perisurgical use of **epoetin alfa** (recombinant human erythropoietin; **EPREX** Janssen-Cilag, New Brunswick, NJ) warrants further investigation as a means of reducing allogeneic blood exposure. The results of an early double-blind study in 41 CABG patients suggested that perisurgical administration of **epoetin alfa** reduces postoperative allogeneic transfusion requirements without causing a significant increase in preoperative hematocrit (Hct). In a double-blind, placebo-controlled, parallel-group study in 182 patients scheduled for coronary artery bypass graft (CABG) surgery, **epoetin alfa** was administered perisurgically by s.c. (SC) injection (150 or 300 IU/kg/d for 5 days prior to surgery, on the day of surgery, and for 2 days postoperatively). All patients received oral iron supplementation for 5 days preoperatively. The intent-to-treat anal. showed that **epoetin alfa** reduced the percentage of patients exposed to allogeneic blood postoperatively compared with placebo, but not significantly. However, when the patients who developed surgical complications were excluded from the anal., the effect of **epoetin alfa** became significant (Fig 1). Reticulocytosis following surgery was significantly increased in patients treated with **epoetin alfa** 300 IU/kg. Although hematocrit (Hct) levels were significantly higher in **epoetin alfa**-treated patients during the first 7 days postoperatively, Hct levels prior to surgery were comparable among **epoetin alfa**- and placebo-treated patients. **Epoetin alfa** was well tolerated, and the overall postoperative mortality rate for patients treated with **epoetin alfa** was similar to that reported in other studies. Perisurgical administration of **epoetin alfa** therefore decreases exposure to allogeneic blood in patients undergoing CABG surgery who do not experience surgical complications. However, the optimum dosage regimen remains to be defined.

IT 113427-24-0, **Epoetin alfa**

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(perioperative **epoetin alfa** reduces transfusion requirements in humans having coronary artery bypass graft surgery)

RN 113427-24-0 HCAPLUS

CN 1-165-Erythropoietin (human clone λ HEPOFL13 protein moiety), glycoform α (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

L108 ANSWER 26 OF 27 HCAPLUS COPYRIGHT 2005 ACS on STN

AN 1996:309220 HCAPLUS

DN 125:2126

TI Subcutaneous **epoetin alfa** as an adjunct to autologous blood donation before elective coronary artery bypass graft surgery

AU Gombotz, Hans

CS Department Anesthesiology, University Graz, Graz, A-8036, Austria

SO Seminars in Hematology (1996), 33(2, Suppl. 2), 69-72

CODEN: SEHEA3; ISSN: 0037-1963

PB Saunders

DT Journal

LA English

AB Autologous blood (AB) donation can minimize exposure to allogeneic blood in patients scheduled for coronary artery bypass graft (CABG) surgery. During AB donation in this group of patients, minimization of the accompanying decrease in Hb levels is important to reduce the risk of provoking silent myocardial ischemia and/or arrhythmias. Recombinant human **erythropoietin** (rHuEPO) has been used to facilitate AB donation and minimize the accompanying decrease in Hb levels in patients scheduled for cardiac surgery. In 24 patients scheduled for CABG surgery, once-weekly s.c. (SC) administration of **rHuEPO** (**epoetin alfa** 400 IU/kg) plus oral **iron** supplementation for 4 wk prior to surgery caused marked stimulation of erythropoiesis and significantly increased collection of autologous red blood cells (RBCs) compared with oral **iron** alone. Furthermore, **epoetin alfa** minimized the decrease in Hb levels associated with AB donation and significantly attenuated allogeneic blood requirements by facilitating the collection of 4 AB units prior to surgery. During AB donation, no changes in the incidence or severity of ischemic attacks or ST-segment changes were observed using electrocardiogram monitoring. **Epoetin alfa** was well tolerated. Once-weekly SC administration of **epoetin alfa** for 4 wk therefore represents a practical means of facilitating AB donation by patients scheduled for CABG surgery.

IT 113427-24-0, **Epoetin alfa**

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(s.c. **epoetin alfa** as an adjunct to autologous blood donation before elective coronary artery bypass graft surgery in humans)

RN 113427-24-0 HCAPLUS

CN 1-165-Erythropoietin (human clone λ HEPOFL13 protein moiety), glycoform α (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

L108 ANSWER 27 OF 27 HCAPLUS COPYRIGHT 2005 ACS on STN

AN 1996:309219 HCAPLUS

DN 125:1483

TI Autologous blood donation with recombinant human **erythropoietin** in cardiac surgery: The Japanese experience

AU Baron, Jean-Francois

CS Service d'Anesthesie Reanimation Chirurgicale, Hopital R. Broussais, Paris, 75674/14, Fr.

SO Seminars in Hematology (1996), 33(2, Suppl. 2), 64-68

CODEN: SEHEA3; ISSN: 0037-1963

PB Saunders

DT Journal; General Review
LA English
AB A review with 9 refs. Four units of predonated autologous blood (AB) is considered sufficient to cover the blood requirements of 95% of patients undergoing elective cardiac surgery, thus avoiding the risks associated with allogeneic blood transfusion. A review of six Japanese studies was undertaken to summarize the potential for recombinant human erythropoietin (rHuEPO) to facilitate donation of AB by patients scheduled for cardiac surgery. I.v. (IV) administration of rHuEPO improved the anemia associated with AB donation, an effect that was further enhanced by IV iron supplementation. Once weekly s.c. (SC) administration of rHuEPO facilitated the donation of AB and reduced allogeneic blood requirements in patients scheduled for cardiac surgery, suggesting that rHuEPO could be administered on an outpatient basis. rHuEPO was of particular benefit in anemic patients, eliminating exposure to allogeneic blood in the majority of patients. In conclusion, rHuEPO facilitates the donation of AB and reduces allogeneic blood requirements of patients scheduled for cardiac surgery.

IT 11096-26-7, Erythropoietin
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(autologous blood donation with recombinant human erythropoietin in Japanese cardiac surgery)

RN 11096-26-7 HCAPLUS
CN Erythropoietin (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

=> fil reg

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DICTIONARY FILE UPDATES: 22 AUG 2005 HIGHEST RN 861291-85-2

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TSCA INFORMATION NOW CURRENT THROUGH JANUARY 18, 2005

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* The CA roles and document type information have been removed from *
* the IDE default display format and the ED field has been added, *
* effective March 20, 2005. A new display format, IDERL, is now *
* available and contains the CA role and document type information. *
*

Structure search iteration limits have been increased. See HELP SLIMITS

for details.

Experimental and calculated property data are now available. For more information enter HELP PROP at an arrow prompt in the file or refer to the file summary sheet on the web at:

<http://www.cas.org/ONLINE/DBSS/registryss.html>

=> => d ide can l112

L112 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2005 ACS on STN

RN 25322-68-3 REGISTRY

ED Entered STN: 16 Nov 1984

CN Poly(oxy-1,2-ethanediyl), α -hydro- ω -hydroxy- (9CI) (CA INDEX NAME)

OTHER NAMES:

CN α , ω -Hydroxypoly(ethylene oxide)

CN α -Hydro- ω -hydroxypoly(oxy-1,2-ethanediyl)

CN α -Hydro- ω -hydroxypoly(oxyethylene)

CN 1,2-Ethanediol, homopolymer

CN 16600

CN 1660S

CN 400DAB8

CN Alkox

CN Alkox E 100

CN Alkox E 130

CN Alkox E 160

CN Alkox E 240

CN Alkox E 30

CN Alkox E 30G

CN Alkox E 45

CN Alkox E 60

CN Alkox E 75

CN Alkox R 100

CN Alkox R 1000

CN Alkox R 15

CN Alkox R 150

CN Alkox R 400

CN Alkox SR

CN Alkox SW

CN Antarox E 4000

CN Aquacide III

CN Aquaffin

CN Badimol

CN BDH 301

CN Bradsyn PEG

CN Breox 2000

CN Breox 20M

CN Breox 4000

CN Breox 550

CN Breox PEG 300

CN CAFO 154

CN Carbowax

CN Carbowax 100

CN Carbowax 1000

CN Carbowax 1350

CN Carbowax 14000

CN Carbowax 1450

CN Carbowax 1500

CN Carbowax 1540

CN Carbowax 20

CN Carbowax 200
 CN Carbowax 20000
 CN Carbowax 25000
 CN Carbowax 300
 CN Carbowax 3350

ADDITIONAL NAMES NOT AVAILABLE IN THIS FORMAT - Use FCN, FIDE, or ALL for
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AR 9002-90-8

DR 615575-04-7, 12676-74-3, 12770-93-3, 9081-95-2, 9085-02-3, 9085-03-4,
 174460-08-3, 174460-09-4, 54510-95-1, 125223-68-9, 54847-64-2, 59763-40-5,
 64441-68-5, 64640-28-4, 133573-31-6, 25104-58-9, 25609-81-8, 134919-43-0,
 101677-86-5, 99264-61-6, 106186-24-7, 112895-21-3, 114323-93-2,
 50809-04-6, 50809-59-1, 119219-06-6, 60894-12-4, 61840-14-0, 37361-15-2,
 112384-37-9, 67411-64-7, 70926-57-7, 75285-02-8, 75285-03-9, 77986-38-0,
 150872-82-5, 154394-38-4, 79964-26-4, 80341-53-3, 85399-22-0, 85945-29-5,
 90597-70-9, 88077-80-9, 88747-22-2, 34802-42-1, 107502-63-6, 107529-96-4,
 116549-90-7, 156948-19-5, 169046-53-1, 188364-77-4, 188924-03-0,
 189154-62-9, 191743-71-2, 196696-84-1, 201163-43-1, 206357-86-0,
 221638-71-7, 225502-44-3, 270910-26-4, 307928-07-0, 356055-70-4,
 391229-98-4

MF (C2 H4 O)_n H2 O

CI PMS, COM

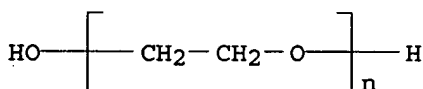
PCT Polyether

LC STN Files: ADISNEWS, AGRICOLA, ANABSTR, AQUIRE, BIOBUSINESS, BIOSIS,
 BIOTECHNO, CA, CABA, CANCERLIT, CAPLUS, CASREACT, CBNB, CEN, CHEMCATS,
 CHEMINFORMRX, CHEMLIST, CHEMSAFE, CIN, CSCHM, CSNB, DDFU, DETHERM*,
 DIOGENES, DRUGU, EMBASE, ENCOMPLIT, ENCOMPLIT2, ENCOMPPAT, ENCOMPPAT2,
 HSDB*, IFICDB, IFIPAT, IFIUDB, IPA, MEDLINE, MRCK*, MSDS-OHS, NIOSHTIC,
 PDLCOM*, PIRA, PROMT, RTECS*, SCISEARCH, SPECINFO, TOXCENTER, TULSA,
 ULIDAT, USAN, USPAT2, USPATFULL, VETU, VTB

(*File contains numerically searchable property data)

Other Sources: DSL**, TSCA**, WHO

(**Enter CHEMLIST File for up-to-date regulatory information)



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

84039 REFERENCES IN FILE CA (1907 TO DATE)

22615 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA

84192 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 143:165633

REFERENCE 2: 143:165571

REFERENCE 3: 143:165272

REFERENCE 4: 143:163889

REFERENCE 5: 143:163879

REFERENCE 6: 143:163722

REFERENCE 7: 143:163291

REFERENCE 8: 143:162547

REFERENCE 9: 143:162006

REFERENCE 10: 143:161849

=> d ide can l111 tot

L111 ANSWER 1 OF 3 REGISTRY COPYRIGHT 2005 ACS on STN

RN 20074-52-6 REGISTRY

ED Entered STN: 16 Nov 1984

CN Iron, ion (Fe3+) (8CI, 9CI) (CA INDEX NAME)

OTHER NAMES:

CN Fe3+

CN Ferric cation

CN Ferric ion

CN Iron (Fe3+)

CN Iron ion(3+)

CN Iron trivalent ion

CN Iron(3+)

CN Iron(3+) ion

CN Iron(III) cation

CN Iron(III) ion

MF Fe

LC STN Files: AGRICOLA, ANABSTR, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CABA, CAPLUS, CASREACT, CHEMCATS, CHEMINFORMRX, CIN, CSNB, DDFU, DETHERM*, DRUGU, EMBASE, IFICDB, IFIPAT, IFIUDB, NIOSHTIC, PIRA, PROMT, TOXCENTER, TULSA, ULIDAT, USPAT2, USPATFULL, VETU
(*File contains numerically searchable property data)

Fe³⁺

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

10606 REFERENCES IN FILE CA (1907 TO DATE)

690 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA

10624 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 143:163763

REFERENCE 2: 143:160506

REFERENCE 3: 143:159768

REFERENCE 4: 143:159477

REFERENCE 5: 143:158665

REFERENCE 6: 143:158192

REFERENCE 7: 143:157906

REFERENCE 8: 143:157868

REFERENCE 9: 143:157295

REFERENCE 10: 143:156829

L111 ANSWER 2 OF 3 REGISTRY COPYRIGHT 2005 ACS on STN

RN 15438-31-0 REGISTRY

ED Entered STN: 16 Nov 1984

CN Iron, ion (Fe2+) (8CI, 9CI) (CA INDEX NAME)

OTHER NAMES:

CN Fe2+

CN Ferrous cation

CN Ferrous ion

CN Iron (Fe2+)

CN Iron dication

CN Iron divalent ion

CN Iron ion(2+)

CN Iron(2+)

CN Iron(II) ion

MF Fe

LC STN Files: ADISNEWS, AGRICOLA, ANABSTR, BIOBUSINESS, BIOSIS, BIOTECHNO,
CA, CABA, CAPLUS, CASREACT, CEN, CHEMCATS, CHEMLIST, CIN, CSNB,
DETERM*, EMBASE, HSDB*, IFICDB, IFIPAT, IFIUDB, NIOSHTIC, PIRA, PROMT,
RTECS*, TOXCENTER, TULSA, ULIDAT, USPAT2, USPATFULL
(*File contains numerically searchable property data)

Fe2+

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

10171 REFERENCES IN FILE CA (1907 TO DATE)

479 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA

10197 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 143:163763

REFERENCE 2: 143:162403

REFERENCE 3: 143:162235

REFERENCE 4: 143:161206

REFERENCE 5: 143:160143

REFERENCE 6: 143:158665

REFERENCE 7: 143:158598

REFERENCE 8: 143:158259

REFERENCE 9: 143:158197

REFERENCE 10: 143:157906

L111 ANSWER 3 OF 3 REGISTRY COPYRIGHT 2005 ACS on STN

RN 7439-89-6 REGISTRY

ED Entered STN: 16 Nov 1984

CN Iron (7CI, 8CI, 9CI) (CA INDEX NAME)

OTHER NAMES:

CN 300A
CN 3ZhP
CN A 131
CN A 227
CN AC 325
CN Ancor B
CN Ancor EN 80/150
CN Ancor Image 100
CN AQ 80
CN Armco 80
CN Armco iron
CN ASC 300
CN ASC 300 (metal)
CN Atomel 300M200
CN Atomel 500M
CN Atomet 28
CN Atomet 95
CN Atomet 95G
CN Atomet 95SP
CN Atomiron 44MR
CN Atomiron 5M
CN Atomiron AFP 25
CN Atomiron AFP 5
CN ATW 230
CN ATW 432
CN BASF-EW
CN Carbon 0.17, iron 99.83 (atomic)
CN Carbonyl iron
CN CM
CN CM (iron)
CN Copy Powder CS 105-175
CN DH
CN DKP
CN DKP (metal)
CN DM 96
CN DM 96 (iron)
CN DNK 2R
CN DSP 1000
CN DSP 128B
CN DSP 135
CN DSP 135C
CN DSP 138
CN EF 1000
CN EF 250
CN EFV
CN EFV 200/300
CN EFV 250
CN EFV 250/400
CN Electrolytic iron
CN EO 5A

ADDITIONAL NAMES NOT AVAILABLE IN THIS FORMAT - Use FCN, FIDE, or ALL for
DISPLAY

DR 8011-79-8, 8053-60-9, 129048-51-7, 73135-38-3, 70884-35-4, 39344-71-3,
190454-13-8, 195161-83-2, 199281-22-6, 443783-52-6, 675141-17-0

MF Fe

CI COM

LC STN Files: ADISNEWS, AGRICOLA, ANABSTR, AQUIRE, BIOBUSINESS, BIOSIS,
BIOTECHNO, CA, CABA, CANCERLIT, CAOLD, CAPLUS, CASREACT, CBNB, CEN,
CHEMCATS, CHEMINFORMRX, CHEMLIST, CIN, CSCHEM, CSNB, DDFU, DETHERM*,
DIOGENES, DIPPR*, DRUGU, EMBASE, ENCOMPLIT, ENCOMPLIT2, ENCOMPPAT,

ENCOMPAT2, HSDB*, IFICDB, IFIPAT, IFIUDB, IPA, MEDLINE, MRCK*,
MSDS-OHS, NIOSHTIC, PIRA, PROMT, RTECS*, TOXCENTER, TULSA, ULIDAT,
USPAT2, USPATFULL, VETU, VTB

(*File contains numerically searchable property data)

Other Sources: DSL**, EINECS**, TSCA**

(**Enter CHEMLIST File for up-to-date regulatory information)

Fe

****PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT****

414329 REFERENCES IN FILE CA (1907 TO DATE)
21949 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
414665 REFERENCES IN FILE CAPLUS (1907 TO DATE)
1 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

REFERENCE 1: 143:165644
REFERENCE 2: 143:165586
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REFERENCE 4: 143:165562
REFERENCE 5: 143:165540
REFERENCE 6: 143:165535
REFERENCE 7: 143:165524
REFERENCE 8: 143:165522
REFERENCE 9: 143:165278
REFERENCE 10: 143:165232

=> d ide can l110 tot

L110 ANSWER 1 OF 15 REGISTRY COPYRIGHT 2005 ACS on STN
RN 702719-62-8 REGISTRY
ED Entered STN: 02 Jul 2004
CN Erythropoietin (human) (9CI) (CA INDEX NAME)
OTHER NAMES:
CN 2: PN: WO2004047858 SEQID: 2 claimed protein
FS PROTEIN SEQUENCE
MF Unspecified
CI MAN
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL

****RELATED SEQUENCES AVAILABLE WITH SEQLINK****

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

*** USE 'SQD' OR 'SQIDE' FORMATS TO DISPLAY SEQUENCE ***

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 141:34188

L110 ANSWER 2 OF 15 REGISTRY COPYRIGHT 2005 ACS on STN
RN 702719-61-7 REGISTRY
ED Entered STN: 02 Jul 2004
CN Erythropoietin (human) (9CI) (CA INDEX NAME)
OTHER NAMES:
CN 1: PN: WO2004047858 SEQID: 1 claimed protein
FS PROTEIN SEQUENCE
MF Unspecified
CI MAN
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL

RELATED SEQUENCES AVAILABLE WITH SEQLINK

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
*** USE 'SQD' OR 'SQIDE' FORMATS TO DISPLAY SEQUENCE ***
1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 141:34188

L110 ANSWER 3 OF 15 REGISTRY COPYRIGHT 2005 ACS on STN
RN 681860-67-3 REGISTRY
ED Entered STN: 14 May 2004
CN Erythropoietin (human 165-amino acid isoform) (9CI) (CA INDEX NAME)
OTHER NAMES:
CN 73: PN: WO2004033651 SEQID: 73 claimed protein
FS PROTEIN SEQUENCE
MF Unspecified
CI MAN
SR CA
LC STN Files: CA, CAPLUS

RELATED SEQUENCES AVAILABLE WITH SEQLINK

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
*** USE 'SQD' OR 'SQIDE' FORMATS TO DISPLAY SEQUENCE ***
1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 140:352406

L110 ANSWER 4 OF 15 REGISTRY COPYRIGHT 2005 ACS on STN
RN 668496-69-3 REGISTRY
ED Entered STN: 29 Mar 2004
CN Erythropoietin (human 166-amino acids variant) (9CI) (CA INDEX NAME)
OTHER NAMES:
CN 2: PN: WO2004019972 SEQID: 2 claimed protein
FS PROTEIN SEQUENCE
MF Unspecified
CI MAN
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL

RELATED SEQUENCES AVAILABLE WITH SEQLINK

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
*** USE 'SQD' OR 'SQIDE' FORMATS TO DISPLAY SEQUENCE ***
1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 140:229921

L110 ANSWER 5 OF 15 REGISTRY COPYRIGHT 2005 ACS on STN
RN 668496-68-2 REGISTRY
ED Entered STN: 29 Mar 2004
CN Erythropoietin (human 165-amino acids variant) (9CI) (CA INDEX NAME)
OTHER NAMES:
CN 1: PN: WO2004019972 SEQID: 1 claimed protein
FS PROTEIN SEQUENCE
MF Unspecified
CI MAN
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL

RELATED SEQUENCES AVAILABLE WITH SEQLINK

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
*** USE 'SQD' OR 'SQIDE' FORMATS TO DISPLAY SEQUENCE ***
1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 140:229921

L110 ANSWER 6 OF 15 REGISTRY COPYRIGHT 2005 ACS on STN
RN 510776-48-4 REGISTRY
ED Entered STN: 06 May 2003
CN 29-165-erythropoietin (human) (9CI) (CA INDEX NAME)
OTHER NAMES:
CN 3: PN: WO03029291 SEQID: 1 claimed protein
FS PROTEIN SEQUENCE
MF Unspecified
CI MAN
SR CA
LC STN Files: CA, CAPLUS, USPAT2, USPATFULL

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
*** USE 'SQD' OR 'SQIDE' FORMATS TO DISPLAY SEQUENCE ***
1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 138:298131

L110 ANSWER 7 OF 15 REGISTRY COPYRIGHT 2005 ACS on STN
RN 510776-47-3 REGISTRY
ED Entered STN: 06 May 2003
CN Erythropoietin (human 166-amino acid isoform) (9CI) (CA INDEX NAME)
OTHER NAMES:
CN 2: PN: WO03029291 SEQID: 2 claimed protein
FS PROTEIN SEQUENCE
MF Unspecified
CI MAN

SR CA
LC STN Files: CA, CAPLUS, USPAT2, USPATFULL

****RELATED SEQUENCES AVAILABLE WITH SEQLINK****

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
*** USE 'SQD' OR 'SQIDE' FORMATS TO DISPLAY SEQUENCE ***
1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 138:298131

L110 ANSWER 8 OF 15 REGISTRY COPYRIGHT 2005 ACS on STN
RN 510776-46-2 REGISTRY
ED Entered STN: 06 May 2003
CN Erythropoietin (human 165-amino acid isoform) (9CI) (CA INDEX NAME)
OTHER NAMES:
CN 1: PN: WO03029291 SEQID: 1 claimed protein
FS PROTEIN SEQUENCE
MF Unspecified
CI MAN
SR CA
LC STN Files: CA, CAPLUS, USPAT2, USPATFULL

****RELATED SEQUENCES AVAILABLE WITH SEQLINK****

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
*** USE 'SQD' OR 'SQIDE' FORMATS TO DISPLAY SEQUENCE ***
1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 138:298131

L110 ANSWER 9 OF 15 REGISTRY COPYRIGHT 2005 ACS on STN
RN 221039-34-5 REGISTRY
ED Entered STN: 08 Apr 1999
CN Erythropoietin (human) (9CI) (CA INDEX NAME)
OTHER NAMES:
CN 1: PN: WO0027869 SEQID: 1 claimed protein
FS PROTEIN SEQUENCE
MF Unspecified
CI MAN
SR CA
LC STN Files: CA, CAPLUS, USPATFULL

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
*** USE 'SQD' OR 'SQIDE' FORMATS TO DISPLAY SEQUENCE ***
5 REFERENCES IN FILE CA (1907 TO DATE)
2 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
5 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 134:91083

REFERENCE 2: 132:352760

REFERENCE 3: 132:31780

REFERENCE 4: 130:357233

REFERENCE 5: 130:218746

L110 ANSWER 10 OF 15 REGISTRY COPYRIGHT 2005 ACS on STN

RN 209810-58-2 REGISTRY

ED Entered STN: 12 Aug 1998

CN Erythropoietin [30-asparagine,32-threonine,87-valine,88-asparagine,90-threonine] (human) (9CI) (CA INDEX NAME)

OTHER NAMES:

CN Aranesp

CN Bone morphogenic protein 7

CN Darbepoetin alfa

CN Darbepoetin alpha

CN erythropoietin [30-asparagine,32-threonine,87-valine,88-asparagine,90-threonine] (human)

CN KRN 321

CN NESP

CN Nespo

CN Ostogenes protein 1

FS PROTEIN SEQUENCE

MF Unspecified

CI MAN

SR CAS Client Services

LC STN Files: ADISINSIGHT, BIOSIS, CA, CANCERLIT, CAPLUS, IMSDRUGNEWS, IMSPATENTS, IMSRESEARCH, IPA, MEDLINE, MRCK*, PATDPASPC, PHAR, PROUSDDR, RTECS*, TOXCENTER, USAN, USPAT2, USPATFULL
(*File contains numerically searchable property data)

RELATED SEQUENCES AVAILABLE WITH SEQLINK

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

*** USE 'SQD' OR 'SQIDE' FORMATS TO DISPLAY SEQUENCE ***

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

134 REFERENCES IN FILE CA (1907 TO DATE)

2 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA

134 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 143:133095

REFERENCE 2: 143:110178

REFERENCE 3: 143:89919

REFERENCE 4: 143:72269

REFERENCE 5: 143:72173

REFERENCE 6: 143:72169

REFERENCE 7: 143:71862

REFERENCE 8: 143:71764

REFERENCE 9: 143:19957

REFERENCE 10: 143:19576

L110 ANSWER 11 OF 15 REGISTRY COPYRIGHT 2005 ACS on STN

RN 134547-95-8 REGISTRY

ED Entered STN: 28 Jun 1991

CN 1-165-Erythropoietin (human clone λ HEPOFL13 protein moiety reduced) (9CI) (CA INDEX NAME)

OTHER NAMES:

CN 1: PN: EP1064951 SEQID: 1 claimed protein

CN 1: PN: WO0102017 SEQID: 1 claimed protein

CN 1: PN: WO0187329 SEQID: 1 claimed protein

CN 2: PN: WO0130320 SEQID: 1 unclaimed protein

CN 4: PN: WO0032772 TABLE: 1 claimed protein

CN Erythropoietin (human 165-amino acid variant)

CN Erythropoietin (human isoform 1)

FS PROTEIN SEQUENCE

MF Unspecified

CI MAN

SR CA

LC STN Files: CA, CAPLUS, IMSPATENTS, IMSRESEARCH, TOXCENTER, USPATFULL

RELATED SEQUENCES AVAILABLE WITH SEQLINK

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

*** USE 'SQD' OR 'SQIDE' FORMATS TO DISPLAY SEQUENCE ***

7 REFERENCES IN FILE CA (1907 TO DATE)

7 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 136:11065

REFERENCE 2: 134:331598

REFERENCE 3: 134:105827

REFERENCE 4: 134:91083

REFERENCE 5: 133:38711

REFERENCE 6: 115:199743

REFERENCE 7: 115:23689

L110 ANSWER 12 OF 15 REGISTRY COPYRIGHT 2005 ACS on STN

RN 122312-54-3 REGISTRY

ED Entered STN: 25 Aug 1989

CN 1-165-Erythropoietin (human clone λ HEPOFL13 protein moiety), glycoform β (9CI) (CA INDEX NAME)

OTHER NAMES:

CN BM 06.019

CN EPOCH

CN Epoetin beta

CN Epogin

CN Marogen

CN NeoRecormon

CN NeoRecormon Multidose Vials

CN Recormon

FS PROTEIN SEQUENCE

MF Unspecified

CI MAN

SR US Adopted Names Council (USAN)

LC STN Files: ADISINSIGHT, ADISNEWS, AGRICOLA, ANABSTR, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CANCERLIT, CAPLUS, CBNB, CIN, CSNB, DDFU,

DIogenES, DRUGU, EMBASE, IMSCoSEARCH, IMSDRUGNEWS, IMSPATENTS,
IMSRSEARCH, IPA, MEDLINE, MRCK*, PIRA, PROMT, PROUSDDR, RTECS*,
SCISEARCH, TOXCENTER, USAN, USPAT2, USPATFULL

(*File contains numerically searchable property data)

Other Sources: WHO

RELATED SEQUENCES AVAILABLE WITH SEQLINK

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

*** USE 'SQD' OR 'SQIDE' FORMATS TO DISPLAY SEQUENCE ***

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

101 REFERENCES IN FILE CA (1907 TO DATE)

101 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 143:120713

REFERENCE 2: 143:72269

REFERENCE 3: 143:1642

REFERENCE 4: 142:476541

REFERENCE 5: 142:404682

REFERENCE 6: 142:397729

REFERENCE 7: 142:367117

REFERENCE 8: 142:148256

REFERENCE 9: 142:107754

REFERENCE 10: 142:16877

L110 ANSWER 13 OF 15 REGISTRY COPYRIGHT 2005 ACS on STN

RN 113427-24-0 REGISTRY

ED Entered STN: 19 Mar 1988

CN 1-165-Erythropoietin (human clone λ HEPOFL13 protein moiety),
glycoform α (9CI) (CA INDEX NAME)

OTHER NAMES:

CN EPO

CN Epoad

CN Epoetin alfa

CN Epogen

CN Eprex

CN Erypo

CN Erypo 4000

CN Espo

CN Procrit

FS PROTEIN SEQUENCE

MF Unspecified

CI MAN

SR US Adopted Names Council (USAN)

LC STN Files: ADISINSIGHT, ADISNEWS, AGRICOLA, BIOBUSINESS, BIOSIS,
BIOTECHNO, CA, CANCERLIT, CAPLUS, CBNB, CEN, CIN, DIogenES, EMBASE,
IMSCoSEARCH, IMSDRUGNEWS, IMSPATENTS, IMSRSEARCH, IPA, MEDLINE, MRCK*,
PATDPASPC, PHAR, PIRA, PROMT, RTECS*, TOXCENTER, USAN, USPAT2, USPATFULL
(*File contains numerically searchable property data)

Other Sources: WHO

RELATED SEQUENCES AVAILABLE WITH SEQLINK

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

*** USE 'SQD' OR 'SQIDE' FORMATS TO DISPLAY SEQUENCE ***

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

306 REFERENCES IN FILE CA (1907 TO DATE)
4 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
306 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 143:133095
REFERENCE 2: 143:127065
REFERENCE 3: 143:127064
REFERENCE 4: 143:120713
REFERENCE 5: 143:72269
REFERENCE 6: 143:72188
REFERENCE 7: 143:71764
REFERENCE 8: 143:53890
REFERENCE 9: 143:53889
REFERENCE 10: 143:53882

L110 ANSWER 14 OF 15 REGISTRY COPYRIGHT 2005 ACS on STN

RN 96024-34-9 REGISTRY

ED Entered STN: 28 Apr 1985

CN Erythropoietin (human clone λ HEPOFL13 protein moiety reduced)
(9CI) (CA INDEX NAME)

OTHER NAMES:

CN 2: PN: EP1064951 SEQID: 2 unclaimed protein

CN 2: PN: WO0102017 SEQID: 2 claimed protein

CN 2: PN: WO0136489 SEQID: 2 claimed protein

CN 2: PN: WO0187329 SEQID: 2 claimed protein

CN Erythropoietin (human 166-amino acid variant)

FS PROTEIN SEQUENCE

MF Unspecified

CI MAN

LC STN Files: CA, CAPLUS, IMSPATENTS, IMSRESEARCH, TOXCENTER, USPATFULL

RELATED SEQUENCES AVAILABLE WITH SEQLINK

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

*** USE 'SQD' OR 'SQIDE' FORMATS TO DISPLAY SEQUENCE ***

24 REFERENCES IN FILE CA (1907 TO DATE)
4 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
24 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 136:11065
REFERENCE 2: 135:4473

REFERENCE 3: 134:105827
REFERENCE 4: 134:91083
REFERENCE 5: 133:38711
REFERENCE 6: 131:139951
REFERENCE 7: 131:73971
REFERENCE 8: 129:27012
REFERENCE 9: 128:320571
REFERENCE 10: 125:50111

L110 ANSWER 15 OF 15 REGISTRY COPYRIGHT 2005 ACS on STN

RN 11096-26-7 REGISTRY

ED Entered STN: 16 Nov 1984

CN Erythropoietin (9CI) (CA INDEX NAME)

OTHER NAMES:

CN Ep

CN EPO

CN Epoetin

CN Epogis S

CN Hempoietine

MF Unspecified

CI COM, MAN

LC STN Files: ADISNEWS, AGRICOLA, ANABSTR, BIOBUSINESS, BIOSIS, BIOTECHNO,
CA, CABA, CANCERLIT, CAPLUS, CBNB, CEN, CHEMCATS, CHEMLIST, CIN, CSCHM,
CSNB, DDFU, DIOGENES, DRUGU, EMBASE, IFICDB, IFIPAT, IFIUDB, IMSPATENTS,
IMSRESEARCH, IPA, MEDLINE, MRCK*, NIOSHTIC, PHAR, PROMT, PROUSDDR,
RTECS*, SCISEARCH, TOXCENTER, USPAT2, USPATFULL, VETU
(*File contains numerically searchable property data)

Other Sources: EINECS**

(**Enter CHEMLIST File for up-to-date regulatory information)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

9386 REFERENCES IN FILE CA (1907 TO DATE)

286 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA

9410 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 143:152011
REFERENCE 2: 143:151887
REFERENCE 3: 143:151885
REFERENCE 4: 143:151210
REFERENCE 5: 143:150640
REFERENCE 6: 143:150628
REFERENCE 7: 143:147793

REFERENCE 8: 143:147789

REFERENCE 9: 143:147736

REFERENCE 10: 143:147566

=> => fil wpix

FILE 'WPIX' ENTERED AT 15:36:08 ON 23 AUG 2005
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FILE LAST UPDATED: 18 AUG 2005 <20050818/UP>
MOST RECENT DERWENT UPDATE: 200553 <200553/DW>
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<http://thomsonderwent.com/support/dwpioref/reftools/classification/code-revision/>
FOR DETAILS. <<<

=> d all abeq tech abex tot 1131

L131 ANSWER 1 OF 5 WPIX COPYRIGHT 2005 THE THOMSON CORP on STN

AN 2002-566640 [60] WPIX

DNC C2002-160608

TI Novel conjugate of erythropoietin glycoprotein with polyethylene
glycol, useful for treating diseases correlated with anemia in chronic
renal failure patients and acquired immunodeficiency syndrome.

DC A25 A96 B04 D16

IN BURG, J; ENGEL, A; FRANZE, R; HILGER, B; SCHURIG, H E; TISCHER, W; WOZNY,
M; BURGERT, J; SHOKOUFANDEH, R

PA (HOFF) HOFFMANN LA ROCHE & CO AG F; (BURG-I) BURG J; (ENGE-I) ENGEL A;
(FRAN-I) FRANZE R; (HILG-I) HILGER B; (SCHU-I) SCHURIG H E; (TISC-I)
TISCHER W; (WOZN-I) WOZNY M

CYC 100

PI WO 2002049673 A2 20020627 (200260)* EN 40 A61K047-48 <--
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ
NL OA PT SD SE SL SZ TR TZ UG ZM ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK
DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR
KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT
RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG UZ VN YU ZA ZM ZW
US 2002115833 A1 20020822 (200262) A61K038-22
AU 2002033230 A 20020701 (200264) A61K047-48 <--

EP 1345628 A2 20030924 (200363) EN A61K047-48 <--
 R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT
 RO SE SI TR

KR 2003074667 A 20030919 (200409) C07K014-505 <--
 BR 2001016381 A 20040225 (200416) A61K047-48 <--
 JP 2004525097 W 20040819 (200455) 68 C07K014-505 <--
 MX 2003005406 A1 20031101 (200468) A61K047-48 <--
 CN 1527726 A 20040908 (200478) A61K047-48 <--
 ZA 2003004647 A 20041124 (200481) 55 A61K000-00

ADT WO 2002049673 A2 WO 2001-EP14434 20011208; US 2002115833 A1 US 2001-14363
 20011211; AU 2002033230 A AU 2002-33230 20011208; EP 1345628 A2 EP
 2001-984811 20011208; WO 2001-EP14434 20011208; KR 2003074667 A KR
 2003-708299 20030619; BR 2001016381 A BR 2001-16381 20011208, WO
 2001-EP14434 20011208; JP 2004525097 W WO 2001-EP14434 20011208, JP
 2002-551010 20011208; MX 2003005406 A1 WO 2001-EP14434 20011208, MX
 2003-5406 20030616; CN 1527726 A CN 2001-820609 20011208; ZA 2003004647 A
 ZA 2003-4647 20030613

FDT AU 2002033230 A Based on WO 2002049673; EP 1345628 A2 Based on WO
 2002049673; BR 2001016381 A Based on WO 2002049673; JP 2004525097 W Based
 on WO 2002049673; MX 2003005406 A1 Based on WO 2002049673

PRAI EP 2000-127891 20001220

IC ICM A61K000-00; A61K038-22; A61K047-48; C07K014-505
 ICS A61K038-18; A61P007-06; A61P013-12; A61P031-18; A61P035-00;
 C07K001-113; C07K014-575; C12P021-02

AB WO 200249673 A UPAB: 20021031

NOVELTY - A conjugate (I) comprising an **erythropoietin** (**EPO**) glycoprotein having an N-terminal alpha -amino group, chosen from human **EPO** (hEPO) or its analogs having sequence of hEPO modified by addition of 1-6 glycosylation sites or a rearrangement of a glycosylation site, where the glycoprotein is covalently linked to a poly(ethylene glycol) group, is new.

DETAILED DESCRIPTION - (I) comprises an **EPO** glycoprotein having an N-terminal alpha -amino group and in vivo biological activity of causing bone marrow cells to increase production of reticulocytes and red blood cells, and chosen from hEPO or its analogs which have sequence of hEPO modified by addition of 1-6 glycosylation sites or a rearrangement of a glycosylation site, where the glycoprotein is covalently linked to a poly(ethylene glycol) group, with the -CO of the poly(ethylene glycol) group forming an amide bond with N-terminal alpha -amino group. The glycoprotein is covalently linked to a poly(ethylene glycol) group of formula (A).

-CO-(CH₂)_x -(OCH₂CH₂)_m-OR (A)

R = methyl;
 x = 2 or 3; and
 m = 450-1350, 550-1000, preferably 650-750.

INDEPENDENT CLAIMS are also included for the following:

- (1) a pharmaceutical composition (II) comprising (I);
- (2) preparing (I);
- (3) a conjugate prepared by the above method; and
- (4) **EPO** glycoproteins comprising a sequence of 165 or 166 amino acids defined in the specification, having a N-terminal peptidic extension which represents a proteolytic cleavage site, optionally comprising a N-terminal purification tag.

ACTIVITY - Antianemic; anti-HIV; cytostatic.
 No supporting data is given.

MECHANISM OF ACTION - None given.

USE - (I) Is useful for preparing medicaments for the treatment and prophylaxis of diseases correlated with anemia in chronic renal failure patients (CRF), acquired immunodeficiency syndrome (AIDS) and for treating cancer patients undergoing chemotherapy (claimed).

(I) Is useful for treating patients by stimulating the division and differentiation of committed erythroid progenitors in the bone marrow.

ADVANTAGE - (I) Has increased circulating half-life and plasma residence time, decreased clearance, increased clinical activity in vivo, improved potency, stability, and area under the curve when compared to unmodified EPO.

Dwg.0/5

FS CPI

FA AB; GI; DCN

MC CPI: A05-H03; A10-E01; A12-V01; B04-C03C;
B04-H07; B04-H0700E; B14-F03; B14-G01; D05-H10;
D05-H17A2

TECH UPTX: 20020919

TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preparation: (I) Is prepared by expressing, preferably serum free fermenting recombinant EPO protein comprising a N-terminal peptidic extension which comprises a proteolytic cleavage sequence, protecting the epsilon-amino groups by citraconylation, proteolytic cleavage of the N-terminal peptidic extension, pegylating the N-terminal alpha-amino group with a compound of formula (B), deprotecting epsilon-amino group of the EPO glycoprotein, and optionally carrying out purification after each of the above steps. The recombinant EPO has a sequence of 165, 166, 174, 169 or 174 amino acids defined in the specification.

R = methyl;

x = 2 or 3; and

m = 450-1350, 550-1000, preferably 650-750.

Preferred Conjugate: (I) has the formula (C).

CH3O(CH2CH2O)m-CH2CH2CH2CO-NH-P (C)

m = 650-750; and

P = a residue of the glycoprotein without the N-terminal alpha-amino group which forms an amide linkage with the poly(ethylene glycol) group.

The glycoprotein is a hEPO expressed by endogenous gene activation. The glycoprotein has the sequence of hEPO modified by a modification chosen from 22 modifications such as Asn30Thr32, Asn51Thr53, Asn57Thr59, Asn69 and Asn69Thr71, or preferably Gln24Ser87Asn88Thr90, Gln38Ser87Asn88Thr90 or Gln83Ser87Asn88Thr90, or by a rearrangement comprising deletion of N-linked glycosylation sites in hEPO and addition of N-linked glycosylation site at position 88 of the sequence of hEPO.

ABEX UPTX: 20020919

ADMINISTRATION - Administered weekly once, at a dose of 0.01-10 mug/kg, preferably 0.1-3 mug/kg. Administration routes not specified.

EXAMPLE - The wild type erythropoietin (EPO) coding fragment was obtained. The coding fragment was amplified using primers EPO-EcoRI and EPO-SalI:

5'-GAGCCTGAATTCACCACC (EPO-EcoRI)

5'-AGGTGGGTCGACCTGGTCATCTGTCCCCTG (EPO-SalI)

The Polymerase Chain Reaction (PCR) fragment was digested and cloned into the multiple cloning site of the pre-digested pCI-dhfr vector fragment.

Expression of EPO gene was under control of the human

cytomegalovirus (CMV) immediate-early enhancer/promoter region, an

optimized chimeric intron for regulated expression and SV40 late

polyadenylation signal. Cloning of APPRIEGR-EPO, APP-EPO

or APPGAAHY-EPO expression constructs were also performed. The

mutagenized cell line Chinese Hamster ovary (CHO)/dhfr-(ATCC CRL-9096)

deficient in the dhfr enzyme gene was obtained. Cells were transfected

with EPO plasmids using the FuGENE6 transfection reagent.

Transfected cells were selected in alpha-MEM lacking nucleosides

(alpha-MEM), supplemented with 10% dialyzed fetal calf serum (FCS), and 2

mM glutamine. Single colonies were isolated by fluorescence activated cell

sorting (FACS), expanded, and the culture supernatants were assayed for

production and secretion of **EPO**. The cells were transferred into glass spinner flasks and cultivated in a hydrogen carbonate-buffered medium in a humidified CO₂ incubator. Typical serum free media was used for the inoculum preparation. After the initial growth period, the cell culture was diluted with fresh medium. After 3-5 days, the culture in the fermenter was used as inoculum for further fermentation. A batch refeed process was used, i.e. when the desired cell density was reached, 80% of the culture was harvested.

The determined harvest was centrifuged, and supernatant was filtered and collected in a second cooled vessel, and purified as described in WO9635718. The solution of the modified **EPO** was adjusted to pH 8.5-9 and stirred. Citraconic anhydride was added slowly to the solution in aliquots, pH of 9 was maintained and stirred. Residual citraconic anhydride was removed by adding 2 M ethanolamine solution. Cleavage of the modified protected **EPO** was achieved by adding cleavage protease or factor Xa. The removal of protease was achieved by size exclusion chromatography. The product was collected in fractions which were pooled according to the purity as analyzed by analytical reverse phase-high pressure liquid chromatography (rpHPLC).

The pooled fractions were concentrated to 7-8 mg/ml, and the pegylation reaction was performed at a molar ratio of 1:5 at a final protein concentration of 5 mg/ml. The pegylation reagent used was a methoxy-polyethylene glycol (PEG)-SBA. The 30 kDa PEG-SBA was dissolved in 1 mM HCl. Protected **EPO** was added and the reaction mixture was stirred. After 2 h, the reaction was stopped by adjusting the pH to 2.5 with acid. The separation of N-terminal pegylated **EPO** from excess reagents, reaction byproducts and non-pegylated **EPO** was achieved by chromatography. The product was collected in fractions which were pooled according to their purity as determined by high performance size exclusion chromatography. The PEG-A1 **EPO** was then concentrated to 4.5-7.5 mg/ml and stored frozen.

L131 ANSWER 2 OF 5 WPIX COPYRIGHT 2005 THE THOMSON CORP on STN

AN 2002-463307 [49] WPIX

DNC C2002-131715

TI Polyethylene glycol-modified **erythropoietin** obtained by chemical modification to lysine residue at 52-position, for use in drug compositions to treat anemia, especially renal anemia.

DC A25 B04 D16

IN KAWATA, H; MACHIDA, M; MIYAMOTO, H; NAKAMURA, T; SEKIMORI, Y

PA (CHUS) CHUGAI SEIYAKU KK; (KAWA-I) KAWATA H; (MACH-I) MACHIDA M; (MIYA-I) MIYAMOTO H; (NAKA-I) NAKAMURA T; (SEKI-I) SEKIMORI Y

CYC 98

PI WO 2002032957 A1 20020425 (200249)* JA 46 C07K014-505 <--
 RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ
 NL OA PT SD SE SL SZ TR TZ UG ZW
 W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK
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 KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PH PL PT RO
 RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
 AU 2001090312 A. 20020429 (200255) C07K014-505 <--
 EP 1333036 A1 20030806 (200353) EN C07K014-505 <--
 R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT
 RO SE SI TR
 JP 2002536338 X 20040226 (200416) C07K014-505 <--
 US 2004082765 A1 20040429 (200429) A61K038-24
 ADT WO 2002032957 A1 WO 2001-JP8539 20010928; AU 2001090312 A AU 2001-90312
 20010928; EP 1333036 A1 EP 2001-970285 20010928, WO 2001-JP8539 20010928;
 JP 2002536338 X WO 2001-JP8539 20010928, JP 2002-536338 20010928; US
 2004082765 A1 WO 2001-JP8539 20010928, US 2003-399254 20030416

FDT AU 2001090312 A Based on WO 2002032957; EP 1333036 A1 Based on WO 2002032957; JP 2002536338 X Based on WO 2002032957

PRAI JP 2000-315421 20001016

IC ICM A61K038-24; C07K014-505

ICS A61K038-22; A61K038-32; A61K047-34; A61K047-48; A61P007-06; A61P043-00; C07K014-23

AB WO 200232957 A UPAB: 20020802

NOVELTY - A mono-polyethylene glycol-modified **erythropoietin** (PEG-modified **EPO**) produced by chemically modifying natural **EPO** with PEG, is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) mono-PEG-modified **EPO** compositions containing the mono-PEG-modified **EPO** and/or a PEG-modified **EPO** of natural **EPO** with 2 or more amino acid residues modified by PEG, 1 molecule of which as determined by gel filtration column chromatography in an aqueous solvent system has an apparent molecular weight of 100-900 kDa;

(2) **EPO** preparations with long-lasting drug effect containing the PEG-modified **EPO** as active ingredient; and

(3) preparing the PEG-modified **EPO** compositions by reacting natural **EPO** with the succinimidyl ester derivative of PEG.

ACTIVITY - Antianemic.

MECHANISM OF ACTION - None given in source material.

USE - The modified **EPO** is for use in drug compositions to treat anemia especially renal anemia.

ADVANTAGE - The **EPO** has enhanced and high long-lasting drug effect but without damage to its physiological activity, which is obtainable by introducing PEG into a controlled binding site at a controlled number of binding molecules. With the formulated drug compositions agents, less nursing and treatment time is needed, less pain and cost to patients too.

DESCRIPTION OF DRAWING(S) - Mapped chromatographic pattern by liquid chromatography after digestion of mono-mPEG-**EPO** with endoprotease Lys-C: with axes of PEG binding site fixation of PEG(1) - **EPO** vs. intact **EPO**(x) (-0.5). (Drawing includes non-English language text).

Dwg.2/14

FS CPI

FA AB; GI; DCN

MC CPI: A10-E01; A12-V01; B04-C03C; B04-H07;

B14-F03; B14-N10; D05-H10

TECH UPTX: 20020802

TECHNOLOGY FOCUS - ORGANIC CHEMISTRY - Preferred Modified **EPO**: Chemical modification with PEG is at the lysine residue at 52-position of natural **EPO**. A mono-PEG-modified **EPO** is obtained by modifying natural **EPO** with a PEG having a molecular weight of 5-40 kDa, one molecule of which as determined by gel filtration column chromatography in an aqueous solvent system has an apparent molecular weight of 100-900 kDa.

ABEX UPTX: 20020802

ADMINISTRATION - Administration is non-oral, e.g. intranasal or by injection at 5-50 microg.

EXAMPLE - A 0.5-ml solution of rh **erythropoietin** (**EPO**) (2.94 mg/ml) in 0.1 mM phosphate buffer at pH 8 was stirred with methoxy polyethylene glycol (PEG)-SPA (succinimidyl propionate; molecular weight of 20 kDa; 3.97 molar ratio), at room temperature for 30 minutes. Then, 10% 0.1 M glycine solution was added to deactivate the ester. After work-up and purification by chromatography on Superdex 200 HR10/30 (RTM),

3.8 mg mono-mPEG-EPO and 1.6 mg di-mPEG-EPO were obtained.

L131 ANSWER 3 OF 5 WPIX COPYRIGHT 2005 THE THOMSON CORP on STN
AN 2002-097323 [13] WPIX
DNC C2002-030219
TI Novel erythropoietin stimulating protein modified by conjugation to a polyethylene glycol moiety has a longer half life than the unmodified form and is useful to treat hematopoietic disorders.
DC A25 A96 B04
IN BOONE, T C; FREEMAN, A; GEGG, C V; KINSTLER, O B; BOONE, T; GEGG, C; KINSTLER, O
PA (AMGE-N) AMGEN INC
CYC 96
PI WO 2001076640 A2 20011018 (200213)* EN 27 A61K047-48 <--
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZW
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AU 2001055256 A 20011023 (200213) A61K047-48 <--
EP 1267942 A2 20030102 (200310) EN A61K047-48 <--
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI TR
US 6586398 B1 20030701 (200345) A61K038-00
US 2003166566 A1 20030904 (200359) A61K038-22
JP 2003530361 W 20031014 (200368) 58 A61K047-48 <--
MX 2002009896 A1 20030301 (200413) A61K047-48 <--
ADT WO 2001076640 A2 WO 2001-US11346 20010406; AU 2001055256 A AU 2001-55256 20010406; EP 1267942 A2 EP 2001-928395 20010406, WO 2001-US11346 20010406; US 6586398 B1 US 2000-545335 20000407; US 2003166566 A1 Cont of US 2000-545335 20000407, US 2003-409807 20030407; JP 2003530361 W JP 2001-574155 20010406, WO 2001-US11346 20010406; MX 2002009896 A1 WO 2001-US11346 20010406, MX 2002-9896 20021007
FDT AU 2001055256 A Based on WO 2001076640; EP 1267942 A2 Based on WO 2001076640; US 2003166566 A1 Cont of US 6586398; JP 2003530361 W Based on WO 2001076640; MX 2002009896 A1 Based on WO 2001076640
PRAI US 2000-545335 20000407; US 2003-409807 20030407
IC ICM A61K038-00; A61K038-22; A61K047-48
ICS A61K038-18; A61P007-06; C07K017-00; C08G063-48; C08G063-91
AB WO 2001076640 A UPAB: 20020226
NOVELTY - A substantially homogenous preparation of chemically modified novel erythropoietin stimulating protein (NESP) is new.
ACTIVITY - anti-anemia
MECHANISM OF ACTION - increases erythropoiesis
USE - The chemically modified NESP is used to treat a hematopoietic disorder (claimed).
ADVANTAGE - The PEGylated NESP has a longer half life and so needs to be administered less frequently than prior art treatment with NESP or rHuEPO.
DESCRIPTION OF DRAWING(S) - Hemoglobin response of normal mice after single bolus injections of 30 mu g/kg 30kD mono-PEG:NESP conjugate (closed triangle), 20kD mono-PEG:NESP conjugate (closed square), 5-kD poly-PEG:NESP conjugate (closed circle) or unmodified NESP (open circle) 5-17 days post treatment.
Dwg.21/22
FS CPI
FA AB; GI; DCN
MC CPI: A12-V01; B04-C03D; B04-N02; B14-F01

TECH

UPTX: 20020226

TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preferred preparation: The NESP is preferably chemically modified with dextran, poly(n-vinyl pyrrolidone), a polyethylene glycol (PEG), a propylene glycol homopolymer, a polypropylene oxide/ethylene oxide co-polymer, a polyoxyethylated polyol or a polyvinyl alcohol, more preferably with PEG with a molecular weight of 2-100kD, more preferably 5-30kD. The preparation may be a mixture of mono-PEGylated and poly-PEGylated NESP and is preferably comprised of at least 95% N-terminally mono-PEGylated NESP and at most 5% unPEGylated NESP. The NESP preferably has the 165 amino acid sequence fully defined in the specification. The PEG moiety is connected to NESP through aldehydes generated in the NESP carbohydrate chains or using methoxy-PEG-NHS chemistry.

ABEX

UPTX: 20020226

ADMINISTRATION - Administration is by intraperitoneal, subcutaneous or intramuscular injection, preferably with iron to maintain increased erythropoiesis. Dosage frequency is once every 4-6 weeks.
 EXAMPLE - 30kD mono-PEG:NESP derived by acylation with the 30kD PEG-NHS ester, 20kD mono-PEG:NESP or 5kD polyPEG:NESP derived by reductive alkylation with the 20kD and 5kD PEG-aldehyde, or unmodified NESP respectively were administered to normal mice as a single bolus subcutaneous dose at 30, 10 or 3 mug/kg. The erythropoietic response and duration was monitored as reticulocyte count or hemoglobin concentration over time. The data showed that all three forms induced a strong erythropoietic response with significant dose reduction, and a prolonged efficacy relative to the unmodified NESP (see figure).

L131 ANSWER 4 OF 5 WPIX COPYRIGHT 2005 THE THOMSON CORP on STN

AN 2001-147051 [15] WPIX

DNC C2001-043438

TI Novel erythropoietin-glycoprotein conjugate useful for treating diseases correlated with anemia in chronic renal failure patients, AIDS and for treating cancer, is linked to polyethylene glycol through linker.

DC A96 B04

IN BURG, J; HILGER, B; JOSEL, H

PA (HOFF) HOFFMANN LA ROCHE & CO AG F; (HOFF) ROCHE DIAGNOSTICS GMBH

CYC 90

PI WO 2001002017 A2 20010111 (200115)* EN 40 A61K047-48 <--
 RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ
 NL OA PT SD SE SL SZ TZ UG ZW
 W: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB
 GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU
 LV MA MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM
 TR TT UA UG UZ VN YU ZA ZW
 AU 2000064299 A 20010122 (200125) A61K047-48 <--
 US 6340742 B1 20020122 (200208) A61K038-18
 NO 2001006304 A 20020219 (200223) A61K047-48 <--
 EP 1196443 A2 20020417 (200233) EN C07K014-505 <--
 R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT
 RO SE SI
 BR 2000012138 A 20020507 (200238) A61K047-48 <--
 KR 2002026514 A 20020410 (200267) C07K014-505 <--
 CN 1359392 A 20020717 (200268) C07K014-505 <--
 HU 2002001971 A2 20020930 (200272) C07K014-505 <--
 CZ 2001004682 A3 20021113 (200282) A61K047-48 <--
 JP 2003503464 W 20030128 (200309) 51 A61K038-22
 ZA 2001010097 A 20030528 (200341) 54 C07K000-00
 MX 2001012974 A1 20020801 (200367) A61K047-48 <--
 AU 768452 B 20031211 (200404) A61K047-48 <--
 NZ 516170 A 20040227 (200418) A61K047-48 <--

EP 1196443 B1 20040526 (200435) EN C07K014-505 <--
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 SI

DE 60011087 E 20040701 (200443) C07K014-505 <--
 RU 2232163 C2 20040710 (200455) C07K014-505 <--
 ES 2220501 T3 20041216 (200506) C07K014-505 <--
 DE 60011087 T2 20050616 (200540) C07K014-505 <--
 IN 2001001842 P4 20050304 (200547) EN C07K014-505 <--

ADT WO 2001002017 A2 WO 2000-EP6009 20000628; AU 2000064299 A AU 2000-64299
 20000628; US 6340742 B1 Provisional US 1999-142243P 19990702, Provisional
 US 1999-147452P 19990805, Provisional US 1999-151454P 19990830, US
 2000-604871 20000628; NO 2001006304 A WO 2000-EP6009 20000628, NO
 2001-6304 20011221; EP 1196443 A2 EP 2000-951312 20000628, WO 2000-EP6009
 20000628; BR 2000012138 A BR 2000-12138 20000628, WO 2000-EP6009 20000628;
 KR 2002026514 A KR 2002-700029 20020102; CN 1359392 A CN 2000-809895
 20000628; HU 2002001971 A2 WO 2000-EP6009 20000628, HU 2002-1971 20000628;
 CZ 2001004682 A3 WO 2000-EP6009 20000628, CZ 2001-4682 20000628; JP
 2003503464 W WO 2000-EP6009 20000628, JP 2001-507507 20000628; ZA
 2001010097 A ZA 2001-10097 20011207; MX 2001012974 A1 WO 2000-EP6009
 20000628, MX 2001-12974 20011214; AU 768452 B AU 2000-64299 20000628; NZ
 516170 A NZ 2000-516170 20000628, WO 2000-EP6009 20000628; EP 1196443 B1
 EP 2000-951312 20000628, WO 2000-EP6009 20000628; DE 60011087 E DE
 2000-00011087 20000628, EP 2000-951312 20000628, WO 2000-EP6009 20000628;
 RU 2232163 C2 WO 2000-EP6009 20000628, RU 2002-102232 20000628; ES 2220501
 T3 EP 2000-951312 20000628; DE 60011087 T2 DE 2000-00011087 20000628, EP
 2000-951312 20000628, WO 2000-EP6009 20000628; IN 2001001842 P4 IN
 2001-CN1842 20011231, WO 2000-EP6009

FDT AU 2000064299 A Based on WO 2001002017; EP 1196443 A2 Based on WO
 2001002017; BR 2000012138 A Based on WO 2001002017; HU 2002001971 A2 Based
 on WO 2001002017; CZ 2001004682 A3 Based on WO 2001002017; JP 2003503464 W
 Based on WO 2001002017; MX 2001012974 A1 Based on WO 2001002017; AU 768452
 B Previous Publ. AU 2000064299, Based on WO 2001002017; NZ 516170 A Based
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 Based on EP 1196443, Based on WO 2001002017; RU 2232163 C2 Based on WO
 2001002017; ES 2220501 T3 Based on EP 1196443; DE 60011087 T2 Based on EP
 1196443, Based on WO 2001002017

PRAI US 1999-151454P 19990830; US 1999-142243P 19990702;
 US 1999-147452P 19990805; US 2000-604871 20000628

IC ICM A61K038-18; A61K038-22; A61K047-48; C07K000-00;
 C07K014-505

ICS A61P007-06; A61P013-12; A61P031-18; A61P035-00

AB WO 200102017 A UPAB: 20010317

NOVELTY - A conjugate (I) comprising, human **erythropoietin**
 glycoprotein (EPO) having at least one free amino group and
 having in vivo biological activity of causing bone marrow cells to
 increase the production of reticulocytes and red blood cells, or its
 analogs, covalently linked to 1-3 lower-alkoxy poly(ethylene glycol)
 groups through a linker (L), is new.

DETAILED DESCRIPTION - (I) comprises **EPO** or its analog
 having primary structure of human **erythropoietin** modified by the
 addition of 1-6 glycosylation sites or by the rearrangement of at least
 one glycosylation site. The glycoprotein is covalently linked to 1-3
 lower-alkoxy poly(ethylene glycol) groups, through a linker of formula
 -C(O)-X-S-Y', with C(O) of the linker forming an amide bond with the free
 amino groups of glycoprotein.

X = -(CH₂)_k- or -CH₂(O-CH₂-CH₂)_k-;
 k = 1-10; and

Y' = (CH₂)₂-SO₂-(CH₂)₂, CH₂C(O)NH(CH₂)₂ or a group of formula (i) or
 (ii).

The average molecular weight of each (PEG) moiety is 20-40

kilodaltons, and molecular weight of (I) is from 51-175 kilodaltons.

INDEPENDENT CLAIMS are also included for the following:

(1) a composition (II) comprising 1-90 % of (I);

(2) a pharmaceutical composition comprising (I) or (II);

(3) preparing (I) or (II) by covalent linking of thiol groups to an **EPO**, and coupling the resulting activated **EPO** with PEG derivative; and

(4) (I) or (II) prepared by the above said method.

ACTIVITY - Antianemic; anti-HIV; cytostatic.

MECHANISM OF ACTION - Enhancer of production of reticulocytes and red blood cells.

Normal healthy mice, 7-15 weeks old, were administered subcutaneously with 0.2 ml of methoxy-PEG-maleimide coupled to **EPO**, unmodified **EPO** and buffer solution. Over a period of 4 days starting 72 hours after the administration, blood was drawn by puncture of the tail vein, diluted and stained with acridine orange staining solution for 3-10 minutes. The reticulocytes were counted. The results showed superior activity and prolonged half life of the pegylated **EPO** species indicated by the significantly increased amounts of reticulocytes and shift of the reticulocytes count maximum using the same dose per mouse.

USE - (I) and (II) are useful for preparation of medicaments for the treatment of prophylaxis of disease correlated with anemia in chronic renal failure patients (CRF), AIDS and for the treatment of cancer patients undergoing chemotherapy. (I) and (II) are also useful for treating the above said diseases (claimed).

Dwg.0/3

FS CPI

FA AB; GI; DCN

MC CPI: A10-E; A10-E08A; A12-V01; A12-W11L; B04-C03C;
B04-H07; B04-N06; B14-A02B1; B14-F03; B14-H01B

TECH UPTX: 20010317

TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preferred Compound: (I) is of formula $P'-(NH-CO-X-S-Y'-(OCH_2CH_2)_m-OR)_n$.

$m = 450-900$;

$n = 1-3$;

R = lower alkyl; and

P' = **EPO** without amino group or amino group which form an amide linkage with X.

P' is also preferably of formula F1 or F2.

X = $(CH_2)_k$ (preferably CH_2);

k = 1-4;

m = 550-800 (preferably 650-700);

n = 1; and

R = CH_3 .

The average molecular weight of PEG is 24-35, preferably 30 kilodaltons.

The glycoprotein is covalently linked to 1 or 2 lower alkoxy e.g. methoxy, capped PEG moieties. **EPO** is expressed by endogenous gene activation. Glycoprotein of **EPO** is modified by N30T32, N51T53, N57T59, N69, N69T71, S68N69T71, V87N88T90, S87N88T90, S87N88G89T90, S87N88T90T92, S87N88T90A162, N69T71S87N88T90, N30T32V87N88T90, N89I90T91, S87N89I90T91, N136T138, N138T140, T125 or P124T125. The glycoprotein has a sequence comprising human **EPO**, and a second sequence at the carboxy terminus of **EPO**, containing at least one glycosylation site. The second sequence comprises a sequence derived from carboxy terminal sequence of human chorionic gonadotropin. The glycoprotein has a sequence SSSSKAPPPSLPSPSRLPGPSDTPILPQ, or a sequence modified by S87N88T90 or N30T32V87N88T90. The glycoprotein has the sequence of **EPO** modified by rearrangement of glycosylation site, preferably deletion of any of the N-linked carbohydrate sites in **EPO** or addition of N-linked carbohydrate site at position 88 of **EPO**. The

glycoprotein has a sequence Q24S87N88T90, Q38S87N88T90, or Q83S87N88T90. Percentage of (I) in (II) is 1-90, preferably 1-96 %.

ABEX

UPTX: 20010317

SPECIFIC SEQUENCES - EPO comprises a sequence of 165 or 166 amino acids fully defined in the specification. The glycoprotein has a sequence SSSSKAPPPSLPSPSRLPGPSDTPILPQ (claimed).

ADMINISTRATION - 0.01-10 (preferably 0.1-1) mug/kg of (I), containing 10-1000 (preferably 50-400) mug/ml of erythropoietin is administered by subcutaneous or intravenous injection.

EXAMPLE - 100 mg erythropoietin glycoprotein (EPO) was activated with SATA. The resulting activated EPO carrying covalently linked blocked thiol groups was separated from by-products like N-hydroxy-succinimide or non-reacted SATA by dialysis. 380 mg methoxy-PEG-maleimide was dissolved in the solution containing 95 mg activated EPO. The resulting molar ratio between activated EPO and methoxy-PEG-maleimide in the solution was 1:4. Covalently linked blocked thiol groups of activated EPO were de-blocked by 1 M aqueous hydroxylamine solution ad 30 mM. The resulting activated EPO in the reaction mixture of the solution contained free thiol (-SH) groups. Deblocking of the thiol groups was followed immediately by coupling between the activated EPO and methoxy-PEG-maleimide for 90 minutes, and 0.2 M aqueous cysteine solution ad 2 mM was added to stop coupling. After 30 minutes excess free thiol groups of the activated EPO were blocked by addition of a 0.5 M N-methylmaleimide solution in DMSO to reach a concentration of 5 mM. After 30 minutes the resulting reaction mixture now containing pegylated EPO species was dialyzed and purified. Content and purity of tri-, di- and mono-pegylated EPO species were evaluated on Coomassie-stained SDS-PAA gels.

L131 ANSWER 5 OF 5 WPIX COPYRIGHT 2005 THE THOMSON CORP on STN

AN 2001-135308 [14] WPIX

DNC C2001-057629

TI New conjugate having modified erythropoietin glycoprotein useful for stimulating red blood cell production and for treating diseases correlated with anemia in chronic renal failure, AIDS or cancer patients.

DC A96 B04

IN BAILON, P S; SEBASTIAN BAILON, P

PA (HOFF) HOFFMANN LA ROCHE & CO AG F; (BAIL-I) BAILON P S; (HOFF) HOFFMANN LA ROCHE INC

CYC 40

PI	NO	2000003372	A	20010103	(200114)*		C07K017-10	
	CA	2310536	A1	20010102	(200114)	EN	C07K014-505	<--
	DE	10031839	A1	20010201	(200114)		C07K014-505	<--
	GB	2353281	A	20010221	(200115)		C07K017-08	
	JP	2001064300	A	20010313	(200118)	16	C07K014-505	<--
	EP	1064951	A2	20010103	(200120)B	EN 16	A61K047-48	<--
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				RO SE SI				
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	FR	2795734	A1	20010105	(200124)		C07K014-505	<--
	HU	2000002553	A2	20010328	(200124)		C12P021-02	
	AU	2000042744	A	20010104	(200128)		C07K014-575	
	CN	1280137	A	20010117	(200128)		C07K014-505	<--
	AU	736067	B	20010726	(200149)		C07K014-575	
	KR	2001049676	A	20010615	(200171)		C07K014-505	<--
	BR	2000002276	A	20011211	(200203)		A61K038-42	
	NZ	505454	A	20011221	(200210)		C07K017-08	
	CZ	2000002386	A3	20020417	(200231)		A61K047-48	<--

SK 2000000987 A3 20020604 (200247) A61K047-48 <--
 SG 92717 A1 20021119 (200303) C07K014-575
 US 6583272 B1 20030624 (200343) C07K014-505 <--
 US 2003120045 A1 20030626 (200343) C07K014-575
 ES 2191511 A1 20030901 (200363) A61K047-48 <--
 IT 1318606 B 20030827 (200374) A61K000-00
 GB 2393960 A 20040414 (200433) C07K017-08
 JP 2004155787 A 20040603 (200436) 23 C07K014-505 <--
 GB 2353281 B 20040609 (200438) C07K017-08
 GB 2393960 B 20040804 (200451) C07K017-08
 CN 1515590 A 20040728 (200469) C07K017-02
 IL 137056 A 20041124 (200504) C07K014-505 <--
 ES 2191511 B1 20050101 (200505) A61K047-48 <--

ADT NO 2000003372 A NO 2000-3372 20000628; CA 2310536 A1 CA 2000-2310536
 20000628; DE 10031839 A1 DE 2000-10031839 20000630; GB 2353281 A GB
 2000-16205 20000630; JP 2001064300 A JP 2000-201525 20000703; EP 1064951
 A2 EP 2000-113115 20000628; ZA 2000003282 A ZA 2000-3282 20000629; FR
 2795734 A1 FR 2000-8609 20000703; HU 2000002553 A2 HU 2000-2553 20000630;
 AU 2000042744 A AU 2000-42744 20000628; CN 1280137 A CN 2000-107889
 20000629; AU 736067 B AU 2000-42744 20000628; KR 2001049676 A KR
 2000-36976 20000630; BR 2000002276 A BR 2000-2276 20000703; NZ 505454 A NZ
 2000-505454 20000628; CZ 2000002386 A3 CZ 2000-2386 20000623; SK
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 6583272 B1 Provisional US 1999-142254P 19990702, Provisional US
 1999-150225P 19990823, Provisional US 1999-151548P 19990831, Provisional
 US 1999-166151P 19991117, US 2000-604938 20000627; US 2003120045 A1
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 19990823, Provisional US 1999-151548P 19990831, Provisional US
 1999-166151P 19991117, Cont of US 2000-604938 20000627, US 2002-293551
 20021114; ES 2191511 A1 ES 2000-1625 20000630; IT 1318606 B IT 2000-MI1479
 20000630; GB 2393960 A Div ex GB 2000-16205 20000630, GB 2004-86 20040105;
 JP 2004155787 A Div ex JP 2000-201525 20000703, JP 2003-419520 20031217;
 GB 2353281 B GB 2000-16205 20000630; GB 2393960 B Div ex GB 2000-16205
 20000630, GB 2004-86 20040105; CN 1515590 A Div ex CN 2000-107889
 20000629, CN 2004-3602 20000629; IL 137056 A IL 2000-137056 20000628; ES
 2191511 B1 ES 2000-1625 20000630

FDT AU 736067 B Previous Publ. AU 2000042744

PRAI US 1999-166151P 19991117; US 1999-142254P 19990702;
 US 1999-150225P 19990823; US 1999-151548P 19990831;
 US 2000-604938 20000627; US 2002-293551 20021114

IC ICM A61K000-00; A61K038-42; A61K047-48; C07K014-505;
 C07K014-575; C07K017-02; C07K017-08; C07K017-10; C12P021-02

ICS A61K038-17; A61K038-18; A61K038-22; A61K039-00; A61P007-00;
 A61P007-06; A61P013-12; A61P031-00; A61P031-18; A61P035-00;
 C07H000-00; C07K001-107; C07K014-59; C07K017-00; C07K019-00;
 C08G065-00; C12N015-12

AB EP 1064951 A UPAB: 20010410 ABEQ treated as Basic
 NOVELTY - A conjugate comprising an **erythropoietin (EPO)**
) glycoprotein is new. The **EPO** has at least one free amino group
 and has the in vivo biological activity of causing bone marrow cells to
 increase production of reticulocytes and red blood cells. The glycoprotein
 is covalently linked to polyethylene glycol groups.
 DETAILED DESCRIPTION - A conjugate comprising an
erythropoietin (EPO) glycoprotein is new. The
EPO has at least one free amino group and has the in vivo
 biological activity of causing bone marrow cells to increase production of
 reticulocytes and red blood cells. The glycoprotein is covalently linked
 to polyethylene glycol groups.
 The **EPO** comprises human **EPO** (hEPO) or its
 analogs, which has the sequence of hEPO modified by the addition of 1-6

glycosylation sites or a rearrangement of at least one glycosylation site.

The glycoprotein is covalently linked to n polyethylene glycol groups of formula $\text{CO}-(\text{CH}_2)_x-(\text{OCH}_2\text{CH}_2)_m-\text{OR}$ (I).

R = lower alkyl;

x = 2 or 3;

m = 450-900 and

n = 1-3.

n And m are chosen so that the molecular weight of the conjugate minus the **erythropoietin** glycoprotein is 20-100 kilodaltons. The CO of each polyethylene glycol group forms an amide bond with one of the amino groups.

INDEPENDENT CLAIMS are also included for the following:

(1) a composition comprising conjugates, each of the conjugates comprising the **erythropoietin** glycoprotein described above, the percentage of conjugates (where n =1) is at least 90% and

(2) preparation of (I).

ACTIVITY - Antianemic; immunostimulant; cytostatic; nephrotropic.

MECHANISM OF ACTION - Bone marrow cell stimulator; erythroid progenitor stimulator.

In separate experiments, a single dose of unmodified **EPO** (25 ng of **EPO**), **PEG(SBA)-EPO** mixture (10 ng of conjugate), mono- and di-pegylated **EPOs** (10 ng conjugate), **PEG(SPA)-EPO** (10 ng of conjugate) and buffer solution were administered to mice. The results showed the superior activity and the prolonged half life of the pegylated **EPO** species indicated by the increased amounts of reticulocytes and the shift of the reticulocytes count maximum using the same dose per mouse (10 ng), compared to a dose of 25 ng for unmodified **EPO**. At 96 h, the amount of reticulocytes for unmodified **EPO**, 30 kDa **PEG(SPA)-EPO**, mono-SBA-**EPO**, di-SBA-**EPO**, **PEG-EPO** conjugate mixture and the control buffer were 500, 1406, 1501, 926, 1338 and 697, respectively. At 144 hours, the number of reticulocytes were approx. 0, 535, 607, 665, 660 and 708, respectively.

USE - Useful for the treating or preventing diseases correlated with anemia in chronic renal failure, AIDS or cancer patients undergoing chemotherapy. The conjugate or composition is also useful for preparing medicaments for the treatment or prophylaxis of these diseases (all claimed).

ADVANTAGE - Compared to unmodified **EPO** and conventional **PEG-EPO** conjugates, the conjugates have an increased circulating half-life and plasma residence time, decreased clearance, and increased clinical activity in vivo.

Dwg.0/0

AB NO 200003372 A UPAB: 20010418

NOVELTY - A conjugate comprising an **erythropoietin (EPO)** glycoprotein is new. The **EPO** has at least one free amino group and has the in vivo biological activity of causing bone marrow cells to increase production of reticulocytes and red blood cells. The glycoprotein is covalently linked to polyethylene glycol groups.

DETAILED DESCRIPTION - A conjugate comprising an **erythropoietin (EPO)** glycoprotein is new. The **EPO** has at least one free amino group and has the in vivo biological activity of causing bone marrow cells to increase production of reticulocytes and red blood cells. The glycoprotein is covalently linked to polyethylene glycol groups.

The **EPO** comprises human **EPO** (hEPO) or its analogs, which has the sequence of hEPO modified by the addition of 1-6 glycosylation sites or a rearrangement of at least one glycosylation site.

The glycoprotein is covalently linked to n polyethylene glycol groups of formula $\text{CO}-(\text{CH}_2)_x-(\text{OCH}_2\text{CH}_2)_m-\text{OR}$ (I).

R = lower alkyl;
x = 2 or 3;
m = 450-900 and
n = 1-3.

n And m are chosen so that the molecular weight of the conjugate minus the **erythropoietin** glycoprotein is 20-100 kilodaltons. The CO of each polyethylene glycol group forms an amide bond with one of the amino groups.

INDEPENDENT CLAIMS are also included for the following:

(1) a composition comprising conjugates, each of the conjugates comprising the **erythropoietin** glycoprotein described above, the percentage of conjugates (where n =1) is at least 90% and

(2) preparation of (I).

ACTIVITY - Antianemic; immunostimulant; cytostatic; nephrotropic.

MECHANISM OF ACTION - Bone marrow cell stimulator; erythroid progenitor stimulator.

In separate experiments, a single dose of unmodified **EPO** (25 ng of **EPO**), PEG(SBA)-**EPO** mixture (10 ng of conjugate), mono- and di-pegylated **EPOs** (10 ng conjugate), PEG(SPA)-**EPO** (10 ng of conjugate) and buffer solution were administered to mice. The results showed the superior activity and the prolonged half life of the pegylated **EPO** species indicated by the increased amounts of reticulocytes and the shift of the reticulocytes count maximum using the same dose per mouse (10 ng), compared to a dose of 25 ng for unmodified **EPO**. At 96 h, the amount of reticulocytes for unmodified **EPO**, 30 kDa PEG(SPA)-**EPO**, mono-SBA-**EPO**, di-SBA-**EPO**, PEG-**EPO** conjugate mixture and the control buffer were 500, 1406, 1501, 926, 1338 and 697, respectively. At 144 hours, the number of reticulocytes were approx. 0, 535, 607, 665, 660 and 708, respectively.

USE - Useful for the treating or preventing diseases correlated with anemia in chronic renal failure, AIDS or cancer patients undergoing chemotherapy. The conjugate or composition is also useful for preparing medicaments for the treatment or prophylaxis of these diseases (all claimed).

ADVANTAGE - Compared to unmodified **EPO** and conventional PEG-**EPO** conjugates, the conjugates have an increased circulating half-life and plasma residence time, decreased clearance, and increased clinical activity in vivo.

Dwg.0/0

FS CPI

FA AB; GI; DCN

MC CPI: A10-E08B; A12-V01; B04-C03C; B04-H07;
B14-F04; B14-G01B

ABEQ EP 1064951 A UPAB: 20010410

NOVELTY - A conjugate comprising an **erythropoietin** (**EPO**) glycoprotein is new. The **EPO** has at least one free amino group and has the in vivo biological activity of causing bone marrow cells to increase production of reticulocytes and red blood cells. The glycoprotein is covalently linked to polyethylene glycol groups.

DETAILED DESCRIPTION - A conjugate comprising an **erythropoietin** (**EPO**) glycoprotein is new. The **EPO** has at least one free amino group and has the in vivo biological activity of causing bone marrow cells to increase production of reticulocytes and red blood cells. The glycoprotein is covalently linked to polyethylene glycol groups.

The **EPO** comprises human **EPO** (h**EPO**) or its analogs, which has the sequence of h**EPO** modified by the addition of 1-6 glycosylation sites or a rearrangement of at least one glycosylation site.

The glycoprotein is covalently linked to n polyethylene glycol groups

of formula $\text{CO}-(\text{CH}_2)_x-(\text{OCH}_2\text{CH}_2)_m-\text{OR}$ (I).

R = lower alkyl;

x = 2 or 3;

m = 450-900 and

n = 1-3.

n And m are chosen so that the molecular weight of the conjugate minus the **erythropoietin** glycoprotein is 20-100 kilodaltons. The CO of each polyethylene glycol group forms an amide bond with one of the amino groups.

INDEPENDENT CLAIMS are also included for the following:

(1) a composition comprising conjugates, each of the conjugates comprising the **erythropoietin** glycoprotein described above, the percentage of conjugates (where n =1) is at least 90% and

(2) preparation of (I).

ACTIVITY - Antianemic; immunostimulant; cytostatic; nephrotropic.

MECHANISM OF ACTION - Bone marrow cell stimulator; erythroid progenitor stimulator.

In separate experiments, a single dose of unmodified **EPO** (25 ng of **EPO**), **PEG(SBA)-EPO** mixture (10 ng of conjugate), mono- and di-pegylated **EPOs** (10 ng conjugate), **PEG(SPA)-EPO** (10 ng of conjugate) and buffer solution were administered to mice. The results showed the superior activity and the prolonged half life of the pegylated **EPO** species indicated by the increased amounts of reticulocytes and the shift of the reticulocytes count maximum using the same dose per mouse (10 ng), compared to a dose of 25 ng for unmodified **EPO**. At 96 h, the amount of reticulocytes for unmodified **EPO**, 30 kDa **PEG(SPA)-EPO**, mono-SBA-**EPO**, di-SBA-**EPO**, **PEG-EPO** conjugate mixture and the control buffer were 500, 1406, 1501, 926, 1338 and 697, respectively. At 144 hours, the number of reticulocytes were approx. 0, 535, 607, 665, 660 and 708, respectively.

USE - Useful for the treating or preventing diseases correlated with anemia in chronic renal failure, AIDS or cancer patients undergoing chemotherapy. The conjugate or composition is also useful for preparing medicaments for the treatment or prophylaxis of these diseases (all claimed).

ADVANTAGE - Compared to unmodified **EPO** and conventional **PEG-EPO** conjugates, the conjugates have an increased circulating half-life and plasma residence time, decreased clearance, and increased clinical activity in vivo.

Dwg.0/0

TECH

UPTX: 20010410

TECHNOLOGY FOCUS - ORGANIC CHEMISTRY - Preparation: Preparation of (I) comprises condensing a polymeric compound of formula (II) with a **EPO** glycoprotein.

Preferred compounds: The conjugate is of formula (IA) or (IB).

P = the residue of the glycoprotein without the n amino group(s), which form amide linkage(s) with the polyethylene glycol group(s);

R = methyl;

m = 650-750 and

n = 1.

The glycoprotein is preferably hEPO, where the hEPO glycoprotein is expressed by endogenous gene activation. The glycoprotein has a sequence comprising 165 amino acids defined in the specification. The glycoprotein has the hEPO sequence, which has a modification selected from the following: Asn30Thr32; Asn51Thr53; Asn57Thr59; Asn69; Asn69Thr71; Ser68Asn69Thr71; Val87Asn88Thr90; Ser87Asn88Thr90; Ser87Asn88Gly89Thr90; Ser87Asn88Thr90Thr92; Ser87Asn88Thr90Ala162; Asn69Thr71Ser87Asn88Thr90; Asn30Thr32Val87Asn88Thr90; Asn89Ile90Thr91; Ser87Asn89Ile90Thr91; Asn136Thr138; Asn138Thr140; Thr125 or Pro124Thr125.

The glycoprotein also has a sequence comprising the hEPO sequence and a second sequence at the carboxy terminus of the human erythropoietin sequence, where the second sequence contains at least one glycosylation site. The second sequence comprises a sequences derived from the carboxy terminal sequence of the human chorionic gonadotropin. The glycoprotein has a sequence selected from:

- (a) the sequence hEPO and the defined 28-amino acid sequence at the carboxy terminus of the hEPO sequence;
- (b) the sequence in (a) modified by Ser87Asn88Thr90; or
- (c) the sequence in (a) modified by Asn30Thr32Val87Asn88Thr90.

The glycoprotein also has the hEPO sequence modified by a rearrangement of at least one glycosylation site, where the rearrangement comprises deletion of any of the N-linked glycosylation sites in human erythropoietin and addition of an N-linked glycosylation site at position 88 of the hEPO sequence. In particular, the hEPO has a modification selected from: Gln24Ser87Asn88Thr90; Gln38Ser87Asn88Thr90; or Gln83Ser87Asn88Thr90.

Preferred composition: The percentage of conjugates in the composition, where n = 1, is at least 92%, preferably 96%.

ABEX

UPTX: 20010410

ADMINISTRATION - The dosage is 0.01-10 (preferably 0.1-1) mug/kg administered once weekly.

EXAMPLE - Erythropoietin (EPO)-producing CHO cell line

(ATCC CRL8695) was prepared. A batch re-feed process was used, i.e. when the desired cell density was reached, 80% of the culture was harvested. The remaining culture was replenished with fresh culture medium and cultivated until the next harvest. The cells were removed by centrifugation or filtration and discarded. The EPO containing supernatant was in-line filtered, collected and purified. The purification of EPO-protein was disclosed in WO96/35718. The purified EPO was subjected to pegylation with mPEG-SBA (II: R = Me; x = 0-3 and m = 650-750)

To 100 mg of EPOsf (9.71 ml of a 10.3 mg/ml EPOsf stock, 5.48 micro-mol), 10 ml of 0.1 M potassium phosphate buffer (pH 7.5) containing 506 mg of 30 kDa methoxy-PEG-SBA (16.5 micro-mol) was added and mixed for 2 hours at room temperature (20-23degreesC). The final protein concentration was 5 mg/ml and the protein:PEG reagent ratio was 1:3. After 2 hours, the reaction was stopped by adjusting the pH to 4.5 with glacial acetic acid and stored at -20degreesC, until ready for purification. The conjugate mixture was purified, then analyzed by SDS-PAGE, and the degree of pegylation determined. The purified conjugate mixture comprised of mono- and di-PEG-EPOsf and was free of unmodified EPOsf as determined by SDS-PAGE analysis. Conjugate mixture comprised 23.4 mg or 78% of the starting material.

=> d his

(FILE 'HOME' ENTERED AT 14:19:58 ON 23 AUG 2005)
SET COST OFF

FILE 'HCAPLUS' ENTERED AT 14:20:07 ON 23 AUG 2005

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L1      1 S US20040209802/PN OR (US2003-706701# OR EP2002-26342)/AP,PRN
        E LEHMAN P/AU
L2      52 S E3-E7,E9-E12
        E LEHMANN P/AU
L3      267 S E3-E6,E11-E14
        E OREDDIGER R/AU
        E ROEDDIGER R/AU

```

jan delaval - 23 august 2005

L4 9 S E3,E4
 E ROEDIGER R/AU
 L5 2 S E4
 E RODIGER R/AU
 L6 1 S E4
 E RODDIGER R/AU
 L7 2 S E4
 E WALTER MATSUI/AU
 L8 4 S E4,E5
 E MATSUI R/AU
 L9 15 S E3
 E MATSUI W/AU
 SEL RN L1

FILE 'REGISTRY' ENTERED AT 14:22:38 ON 23 AUG 2005

L10 7 S E1-E7
 L11 6 S L10 AND ERYTHROPOIETIN
 L12 1 S L10 NOT L11
 E ERYTHROPOIETIN
 L13 1792 S E3
 L14 1792 S L11,L13
 E IRON/CN
 L15 1 S E3
 E FE/MF
 L16 30 S E3 NOT MASS
 L17 30 S L15,L16

FILE 'HCAPLUS' ENTERED AT 14:24:56 ON 23 AUG 2005

L18 9810 S L14
 L19 11804 S ?ERYTHROPOIETIN?
 L20 129 S DARBEPOETIN?(S) (ALPHA OR ALFA)
 L21 135 S ?DARBEPOETIN?
 L22 6067 S EPO OR EPREX
 L23 298 S EPOETIN?(S) (ALFA OR ALPHA)
 L24 100 S EPOETIN?(S) BETA
 L25 458 S EPOETIN
 L26 42 S ARANESP
 L27 14463 S L18-L26
 L28 655 S L27 AND L17
 L29 1236 S L27 AND (FE OR IRON)
 L30 1243 S L28,L29
 E HEART DISEASE/CT
 E E4+ALL
 E E2+ALL
 L31 86736 S E7+OLD,NT
 L32 29 S L30 AND L31
 L33 0 S E90+OLD,NT AND L30
 L34 47 S E92+OLD,NT AND L30
 L35 36 S L32,L34 AND (PY<=2002 OR PRY<=2002 OR AY<=2002)
 L36 1 S L32,L34 AND L1-L9
 L37 3 S L35 AND ?CONJUGAT?
 L38 2 S L37 NOT 3/SC
 L39 2 S L36,L38
 L40 33 S L35 NOT L36-L39
 SEL DN AN 6-9 13-15 19-27
 L41 16 S L40 AND E1-E48
 L42 18 S L39,L41
 L43 597 S ?RHUEPO?
 L44 155 S L43 AND (L17 OR FE OR IRON)
 L45 3 S L44 AND L31

E HEART, DISEASE/CT
E E3+ALL
L46 5 S L44 AND E92+OLD,NT
L47 5 S L45,L46
L48 4 S L47 NOT 2005/PY
L49 19 S L42,L48 AND L1-L9,L18-L48
L50 14474 S L27,L43
L51 360 S L50 AND ?CONJUGAT?
L52 330 S L50 AND ?GLYCOSYLAT?
L53 194 S L50 AND (PEG OR PEGYLAT?)
L54 55 S L50 AND (POLYOXYETHYLENE OR POLYETHYLENEGLYCOL OR POLYETHYLEN
L55 4 S L50 AND POLY() (OXYETHYLENE OR ETHYLENEGLYCOL OR ETHYLENEOXIDE
L56 24 S L50 AND POLY() (OXY ETHYLENE OR ETHYLENE GLYCOL OR ETHYLENE OX
L57 237 S L50 AND (POLYOXY ETHYLENE OR POLYETHYLENE GLYCOL OR POLYETHYL
L58 316 S L50 AND POLYOXYALKYLENE

FILE 'REGISTRY' ENTERED AT 14:42:28 ON 23 AUG 2005

L59 1 S 25322-68-3
L60 0 S L14 AND C2H4O

FILE 'HCAPLUS' ENTERED AT 14:42:46 ON 23 AUG 2005

L61 266 S L50 AND L59
L62 986 S L51-L58,L61
L63 804 S L62 AND (PY<=2002 OR PRY<=2002 OR AY<=2002)
L64 32 S L63 AND (L17 OR FE OR IRON)
L65 30 S L64 AND L18

FILE 'REGISTRY' ENTERED AT 14:44:41 ON 23 AUG 2005

L66 1 S L14 AND NC4/ES
L67 11 S L14 AND S/ELS

FILE 'HCAPLUS' ENTERED AT 14:45:59 ON 23 AUG 2005

L68 12350 S L27 AND (PY<=2002 OR PRY<=2002 OR AY<=2002)
L69 1036 S L68 AND (L17 OR FE OR IRON)
L70 1808 S L63-L65,L69
L71 1808 S L70 OR L70
L72 500 S L71 RAN=(2001:686932,)
L73 500 S L71 RAN=(1997:740129,2001:679500)
L74 808 S L71 RAN=(,1997:730870)

FILE 'REGISTRY' ENTERED AT 14:48:11 ON 23 AUG 2005

FILE 'HCAPLUS' ENTERED AT 14:48:17 ON 23 AUG 2005

SET SMARTSELECT ON
L75 SEL L74 1- RN : 3039 TERMS
SET SMARTSELECT OFF

FILE 'REGISTRY' ENTERED AT 14:48:35 ON 23 AUG 2005

L76 3035 S L75

FILE 'HCAPLUS' ENTERED AT 14:48:58 ON 23 AUG 2005

SET SMARTSELECT ON
L77 SEL L73 1- RN : 4980 TERMS
SET SMARTSELECT OFF

FILE 'REGISTRY' ENTERED AT 14:49:13 ON 23 AUG 2005

L78 4980 S L77

FILE 'HCAPLUS' ENTERED AT 14:49:40 ON 23 AUG 2005

SET SMARTSELECT ON

L79 SEL L72 1- RN : 43982 TERMS
SET SMARTSELECT OFF

FILE 'REGISTRY' ENTERED AT 14:50:18 ON 23 AUG 2005

L80 43982 S L79
L81 49174 S L76,L78,L80
L82 455 S L81 AND C2H4O
L83 55 S L82 AND NC4/ES
L84 1 S L83 AND S/ELS
L85 54 S L83 NOT L84
L86 STR
L87 50 S L86
L88 STR L86
L89 50 S L88
L90 15844 S L86 FUL
L91 86 S L90 AND C2H4O
L92 28 S L91 AND 1/NR NOT P/ELS
SEL RN 4 6-9 22 28
L93 7 S L92 AND E1-E7
L94 58 S L91 NOT L92
L95 35 S L94 NOT P/ELS

FILE 'HCAPLUS' ENTERED AT 15:13:34 ON 23 AUG 2005

L96 8 S L93
L97 0 S L96 AND L50
L98 136 S L51,L52 AND L53-L58,L61
L99 110 S L98 AND (PY<=2002 OR PRY<=2002 OR AY<=2002)
L100 18 S L99 AND L51 AND L52
L101 0 S L100 AND L31
L102 6 S L98 AND L31
L103 4 S L99 AND L31
L104 6 S L102,L103
L105 18 S L100 NOT L104
SEL DN AN 3 7 9 12 13 15 16 17
L106 8 S E8-E31 AND L105
SEL DN AN L48 1 4
L107 2 S L48 AND E32-E37
L108 27 S L49,L106,L107
SEL HIT RN

FILE 'REGISTRY' ENTERED AT 15:23:50 ON 23 AUG 2005

L109 19 S E38-E56
L110 15 S L109 AND L14
L111 3 S L109 AND L17
L112 1 S L109 AND L59

FILE 'HCAPLUS' ENTERED AT 15:25:04 ON 23 AUG 2005

FILE 'REGISTRY' ENTERED AT 15:25:36 ON 23 AUG 2005

FILE 'WPIX' ENTERED AT 15:26:21 ON 23 AUG 2005

L113 1961 S L19/BI,ABEX OR L20/BI,ABEX OR L21/BI,ABEX OR L22/BI,ABEX OR L
L114 570 S (B04-H07 OR C04-H07)/MC
E ERYTHROPOIETIN/CN
L115 7 S E3-E9
E DARBEPOETIN/CN
L116 1 S E4,E5
L117 8 S L115,L116
SEL SDCN
EDIT /SDCN /DCN

L118 653 S E1-E8
L119 213 S C07K014-505/IPC
L120 2084 S L113,L114,L118,L119
L121 101 S L120 AND A61K047-48/IPC
L122 29 S L120 AND A05-H03?/MC
L123 98 S L120 AND (B04-C03C OR C04-C03C)/MC
E PEG/CN
L124 2 S E3
L125 10737 S (RA0GM6 OR R02044)/DCN OR 2044/DRN
L126 136 S L120 AND L125
L127 33 S L121 AND L122,L123,L126
L128 2 S L127 AND A61P009/IPC
L129 14 S L127 AND (B14-F? OR C14-F? OR B12-F? OR C12-F?)/MC
L130 15 S L128,L129
SEL DN AN 6 7 9 11 12
L131 5 S E1-E10 AND L130

FILE 'WPIX' ENTERED AT 15:36:08 ON 23 AUG 2005

=>

GenCore version 5.1.6
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OM protein - protein search, using sw model

Run on: August 23, 2005, 13:52:33 ; Search time 39 Seconds

(without alignments)
407.071 Million cell updates/sec

Title: US-10-706-701-1

Perfect score: 846

Sequence: 1 APPRLICDSRVLEAK.....SNFLRGKLYTGEACRTGD 165

Scoring table: BLOSUM62

Gapop 10.0 , Gapext 0.5

Searched: 283416 seqs, 96216763 residues

Total number of hits satisfying chosen parameters: 283416

Minimum DB seq length: 0

Maximum DB seq length: 2000000000

Post-processing: Minimum Match 0%

Maximum Match 100%

Listing first 45 summaries

Database :

1: PIR.79.*

2: PIR1.*

3: PIR2.*

4: PIR3.*

5: PIR4.*

Pred. No. is the number of results predicted by chance to have a score greater than or equal to the score of the result being printed, and is derived by analysis of the total score distribution.

SUMMARIES

Result No.	Score	Query Match	Length	DB ID	Description
1	846	100.0	193	1 ZHUH	erythropoietin pre
2	764.5	90.4	192	1 JQ0173	erythropoietin pre
3	759.5	89.8	192	1 I84613	erythropoietin pre
4	713	84.3	188	1 I46083	erythropoietin pre
5	701	82.9	192	1 S28148	erythropoietin pre
6	685.5	81.0	194	1 I46401	erythropoietin pre
7	681	80.5	192	1 A24902	erythropoietin pre
8	680.5	80.4	195	2 JG7699	erythropoietin - r
9	678	80.1	190	2 I46578	erythropoietin - p
10	638	75.4	175	2 I46199	erythropoietin - d
11	90	10.6	353	2 G02729	thrombopoietin - h
12	89	10.5	353	2 I80105	thrombopoietin pre
13	88	10.4	323	2 AB0323	ribonucleoside-dip
14	87.5	10.3	346	2 AS0959	Solute binding rec
15	86	10.2	286	2 AS5530	megakaryocyte grow
16	83	9.8	296	2 A10443	probable 2-hydroxy
17	83	9.8	339	2 A83274	UDP-N-acetylpyruvo
18	80.5	9.5	3033	1 GNMVJ8	genome polyprotein
19	79.5	9.4	1829	2 T35681	probable sensory h
20	79	9.3	480	2 S56639	ribosomal protein
21	78.5	9.3	813	2 A90526	ATP-dependent heli
22	78.5	9.3	897	2 A54696	EGF receptor subst
23	78	9.2	348	2 T35450	ABC transporter AT
24	78	9.2	455	2 AG2919	conserved hypothet
25	78	9.2	455	2 H97693	methylamine utiliz
26	77.5	9.2	747	1 S36741	probable copper-tr
27	77.5	9.2	242	2 A01928	hypothetical prote
28	77	9.1	451	2 S75569	hypothetical prote
29	76.5	9.0	154	2 H82810	bacterioferritin X

30	76.5	9.0	425	2 AB3465	mandelate racemase
31	75.5	8.9	637	2 S75772	hypothetical prote
32	74.5	8.8	400	2 AB2922	conserved hypothet
33	74.5	8.8	425	2 C97696	rtS beta (AF305057
34	74.5	8.8	824	2 D64738	ATP-dependent heli
35	74	8.7	282	2 B37994	RF2 protein - saim
36	74	8.7	326	2 JC4125	thrombopoietin pre
37	74	8.7	335	2 AH3625	ribonucleoside-dip
38	74	8.7	1564	2 S55517	probable transport
39	73.5	8.7	401	2 H83911	hypothetical prote
40	73.5	8.7	476	1 S71789	GCNS protein - hum
41	73.5	8.7	717	2 F82613	VacB protein XF198
42	73	8.6	263	2 B75361	WD-repeat family p
43	73	8.6	1089	2 S53978	PSB1 protein - yea
44	72.5	8.6	379	2 H69478	NADH2 dehydrogenas
45	72.5	8.6	401	2 AF3341	precorrin-6y C5,15

ALIGNMENTS

RESULT 1

ZUHU

erythropoietin precursor [validated] - human

C:Species: Homo sapiens (man)

C>Date: 27-Nov-1985 #sequence revision 27-Nov-1985 #text_change 09-Jul-2004

C:Accession: A01855; A24744; A25384; A22210; S56178

R:Jacobs, K.; Shoemaker, C.; Rudersdorf, R.; Neill, S.D.; Kaufman, R.J.; Mufson, A.; Se Nature 313, 806-810, 1985

A:Title: Isolation and characterization of genomic and cDNA clones of human erythropoie

A:Reference number: A01855; MUID:85137899; PMID:3838366

A:Accession: A01855

A:Molecule type: mRNA; DNA

A:Residues: 1-193 <JAC>

R:Lin, F.K.; Suggs, S.; Lin, C.H.; Browne, J.K.; Smalling, R.; Egrie, J.C.; Chen, K.K.;

Proc. Natl. Acad. Sci. U.S.A. 82, 7580-7584, 1985

A:Title: Cloning and expression of the human erythropoietin gene.

A:Reference number: A24744; MUID:86067948; PMID:3865178

A:Accession: A24744

A:Molecule type: DNA

A:Residues: 1-193 <LIN>

A:Cross-references: GB:M11319; NID:G182197; PIDN:AAA52400.1; PID:G182198

R:Lai, P.H.; Everett, R.; Wang, F.F.; Arakawa, T.; Goldwasser, E.

J. Biol. Chem. 261, 3116-3121, 1986

A:Title: Structural characterization of human erythropoietin.

A:Reference number: A25384; MUID:86140080; PMID:3949763

A:Accession: A25384

A:Molecule type: protein

A:Residues: 28-86, 'Q', 87-193 <LAI>

A:Experimental source: urine

A:Note: forms without the carboxyl-terminal residue and the four carboxyl-terminal resi

R:Yanagawa, S.; Hirade, K.; Ohnata, H.; Sasaki, R.; Chiba, H.; Ueda, M.; Goto, M.

J. Biol. Chem. 259, 2707-2710, 1984

A:Title: Isolation of human erythropoietin with monoclonal antibodies.

A:Reference number: A22210; MUID:84135751; PMID:6698989

A:Accession: A22210

A:Molecule type: protein

A:Residues: 28-29, 'X', 31-33, 'L', 35-50, 'X', 52-53, 'D', 55, 'G', 57 <YAN>

R:Matsumoto, S.; Ikura, K.; Ueda, M.; Sasaki, R.

Plant Mol. Biol. 27, 1163-1172, 1995

A:Title: Characterization of a human glycoprotein (erythropoietin) produced in cultured

A:Reference number: S56178; MUID:95284365; PMID:7766897

A:Accession: S56178

A:Molecule type: protein

A:Residues: 28-33, 'X', 35-37 <MTS>

C:Comment: Erythropoietin is produced by kidney or liver of adult mammals and by liver

C:Genetics:

A:Gene: GDB:EPO

A:Cross-references: GDB:119110; OMIM:133170

A:Map position: 7q21.3-q22.1

A:Introns: 5/1; 53/3; 82/3; 142/3

C:Function:

A;Residues: 1-194 <FX>
A;Cross-references: UNIPROT:P33709; EMBL:Z24681; NID:g395049; PIDN:CAA80848.1; PID:g39593
R;Wen, D.; Boissel, J.
Blood 82, 1507-1516, 1993
A;Title: Erythropoietin structure-function relationships: High degree of sequence homol
A;Reference number: I46083; MUID:93372347; PMID:8364201
A;Accession: I47077
A;Status: translated from GB/EMBL/DBJ
A;Molecule type: mRNA
A;Residues: 4-15, 'L', 17-107, 'P', 109-194 <WEN>
A;Cross-references: GB:L10610; NID:g165876; PIDN:AAA31518.1; PID:g165877
C;Comment: Erythropoietin is produced by kidney or liver of adult mammals and by liver
C;Function:
A;Description: the primary inducer of erythrocyte formation
C;Superfamily: erythropoietin
C;Keywords: erythropoiesis; glycoprotein; hormone; kidney; liver
F;1-27/Domain: signal sequence #status predicted <SIG>
F;28-194/Product: erythropoietin #status predicted <MAT>
F;34-189,55-60/Disulfide bonds: #status predicted
F;51,65,110/Binding site: carbohydrate (Asn) (covalent) #status predicted
F;154/Binding site: carbohydrate (Ser) (covalent) #status predicted

Query Match 81.0%; Score 685.5; DB 1; Length 194;
Best Local Similarity 81.9%; Pred.No. 3.9e-58;
Matches 136; Conservative 9; Mismatches 20; Indels 1; Gaps 1;

Qy 1 APPRLCDSRVRLRYLLAEAEENITTCGAHCSLNNENITVPDTKVNFWAKRMEVQQA 60
Db 28 APPRLCDSRVRLRYLLAEAEENITTCGAHCSLNNENITVPDTKVNFWAKRMEVQQA 87
Qy 61 VFWQGLALLSEAVLRGQALLVNSQPWEPLQHVDKAVSGLRSLTLLRALGAKQKAIS 120
Db 88 LEVWQGLALLSEAVIRGQALLANASQCEALRLHVDKAVSGLRSLTLLRALGAKQKAIP 147
Qy 121 PPDAASAPLRITITADTRFKLFRVYSNPLRGKLYLTGTGACRTGD 165
Db 148 LPDATPSAAPLRITFTVDALSKLFRVYSNPLRGKLYLTGTGACRRGD 193

RESULT 7
A24902
erythropoietin precursor - mouse
C;Species: Mus musculus (house mouse)
C;Date: 25-Oct-1987 #sequence_revision 15-Nov-1996 #text_change 09-Jul-2004
C;Accession: A24902; A24901
R;Shoenmaker, C.B.; Mitsock, L.D.
Mol. Cell. Biol. 6, 849-858, 1986
A;Title: Murine erythropoietin gene: cloning, expression, and human gene homology.
A;Reference number: A24902; MUID:87039105; PMID:3773894
A;Accession: A24902
A;Molecule type: DNA
A;Residues: 1-192 <SHO>
A;Cross-references: UNIPROT:P07321
A;Note: the authors translated the codon TTA for residue 12 as Phe, TTA for residue 43
R;McDonald, J.D.; Lin, F.K.; Goldwasser, E.
Mol. Cell. Biol. 6, 842-848, 1986
A;Title: Cloning, sequencing, and evolutionary analysis of the mouse erythropoietin gen
A;Reference number: A24901; MUID:87039104; PMID:3022133
A;Accession: A24901
A;Molecule type: DNA
A;Residues: 1-67, 'P', 69-192 <MCD>
A;Cross-references: GB:M12930; NID:g193086; PIDN:AAA37570.1; PID:g387152
C;Comment: Erythropoietin is produced by kidney or liver of adult mammals and by liver
C;Genetics:
A;Introns: 5/1; 52/3; 81/3; 141/3
C;Function:
A;Description: the primary inducer of erythrocyte formation
C;Superfamily: erythropoietin
C;Keywords: erythropoiesis; glycoprotein; hormone; kidney; liver
F;1-26/Domain: signal sequence #status predicted <SIG>
F;27-192/Product: erythropoietin #status predicted <MAT>
F;33-187,55-165/Disulfide bonds: #status predicted
F;50,64,109/Binding site: carbohydrate (Asn) (covalent) #status predicted

Qy 1 APRRLICDSRLVRLYLEAKEAENITTCGAHCHSLENENITVPDTKVFNFKRMEVGQQA 60
Db 24 APP--ACDLRLVSKGLRSHVLSKLSQCPEVHPLPTPVLLPAVDPSLGKWKQMEETKA 81
Qy 61 VEWQCIALLSEAVL--RGQALLVNSQPWPEPLQLHVDKAVSGLRSLTLLRALGAQKEA 118
Db 82 QDILGNVTLLEGVMAARGQLGPTCLSSILGQSEQVRLLLGALQSL-----LGTQ--- 132
Qy 119 ISPPDAASAAPLRTITADTRFKLFRVYSNFLRGKLGK 154
Db 133 -LPPOG-----RTTAHKDQNAIFLSFOHLLRGKVR 161
RESULT 12
180105
N:thrombopoietin precursor - human
C:Species: Homo sapiens (man)
C:Date: 24-May-1996 #sequence_revision 24-May-1996 #text_change 09-Jul-2004
C:Accession: 159281; 180105; S45331; S48740; 138672; 152610
R:Poster, D.C.; Sprecher, C.A.; Grant, F.J.; Kramer, J.M.; Kuijper, J.L.; Holly, R.D.; W.
Proc. Natl. Acad. Sci. U.S.A. 91, 13023-13027, 1994
A:Title: Human thrombopoietin: gene structure, cDNA sequence, expression, and chromosome
A:Reference number: 159281; MUID:95108091; PMID:7809166
A:Accession: 159281
A:Status: translated from GB/EMBL/DDBJ
A:Molecule type: DNA
A:Residues: 1-353 <RE2>
A:Cross-references: UNIPROT:P40225; GB:L36051; NID:G533214; PIDN:AAC37568.1; PID:G533215
A:Accession: 180105
A:Status: translated from GB/EMBL/DDBJ
A:Molecule type: mRNA
A:Residues: 1-353 <RE3>
A:Cross-references: GB:L36052; NID:G533216; PIDN:AAC37566.1; PID:G533217
R:de Sauvage, F.J.; Hass, P.E.; Spencer, S.D.; Malloy, B.E.; Gurney, A.L.; Spencer, S.A.
D.V.; Eaton, D.L.
Nature 369, 533-538, 1994
A:Title: Stimulation of megakaryocytopoiesis and thrombopoiesis by the c-Mpl ligand.
A:Reference number: S45331; MUID:94261202; PMID:8202154
A:Accession: S45331
A:Status: preliminary
A:Molecule type: mRNA
A:Residues: 1-353 <SAU>
A:Cross-references: GB:L33410; NID:G506826; PIDN:AAAS9857.1; PID:G506827
R:Shoma, Y.; Akahori, H.; Seki, N.; Horii, T.; Ogami, K.; Kato, T.; Shimada, Y.; Kawamura
FEBS Lett. 353, 57-61, 1994
A:Title: Molecular cloning and chromosomal localization of the human thrombopoietin gene
A:Reference number: S48740; MUID:95010765; PMID:7926023
A:Accession: S48740
A:Status: preliminary
A:Molecule type: DNA
A:Residues: 1-353 <SOH>
A:Cross-references: GB:D32046; NID:G577319; PIDN:BAA06807.1; PID:G577320
R:Bartley, T.D.; Bogenberger, J.; Hunt, P.; Li, Y.S.; Lu, H.S.; Martin, F.; Chang, M.S.;
Cell 77, 1117-1124, 1994
A:Title: Identification and cloning of a megakaryocyte growth and development factor tha
A:Reference number: A54463; MUID:94291201; PMID:8020099
A:Accession: 138672
A:Status: preliminary
A:Molecule type: mRNA
A:Residues: 1-112, 'E', 114-353 <RE3>
A:Cross-references: EMBL:U11025; NID:G511223; PIDN:AAA50553.1; PID:G558078
R:Gurney, A.L.; Kuang, W.J.; Xie, M.H.; Malloy, B.E.; Eaton, D.L.; de Sauvage, F.J.
Blood 85, 981-988, 1995
A:Title: Genomic structure, chromosomal localization, and conserved alternative splice f
A:Reference number: 152610; MUID:95152076; PMID:7849319
A:Accession: 152610
A:Status: preliminary
A:Molecule type: DNA
A:Residues: 1-353 <RE4>
A:Cross-references: GB:S76771; NID:G914225; PIDN:AAB33390.1; PID:G914226
C:Genetics:
A:Gene: GDB:THPO; MGDP

A;Cross-references: GDB:374007; OMIM:600044
A;Map position: 3q26.3-3q27
A;Introns: 5/1; 47/3; 76/3; 132/3
C;Keywords: alternative splicing; cytokine; glycoprotein

Query Match 10.5%; Score 89; DB 2; Length 353;
Best Local Similarity 26.3%; Pred. No. 0.86;
Matches 41; Conservative 20; Mismatches 75; Indels 20; Gaps 5;

Qy 1 APPRLICDSRVLERLYLLEAKAEENITTCGCAEHCSLNENITVPDKVNFYAWKRMVEVGQA 60
||| ||| : : : : : : : : : : : : : : : :
Db 24 APP--ACDLRVLSKLLRDHSVILSRLSQCDEVHPLPTFVLLPAVDPSLGWKTOBETKA 81
||| ||| : : : : : : : : : : : : : : : :
Qy 61 VEVWQGALLSEAVL--RGOALLVNSSQPWEPLQLHVDKAVSGLRSLTTLRALGAQKEA 118
:: : : : : : : : : : : : : : : :
Db 82 QDILGAVTLLLEGVMARGLGPCTCLSSLLGQLSGVRRLLLGALQSL-----LGTQ--- 132
||| ||| : : : : : : : : : : : : : : : :
Qy 119 ISPPDAASAAPLTRITADTFRKLPFRVYSNFLRGKLK 154
||| ||| : : : : : : : : : : : : : : : :
Db 133 -LPFG-----RTTAHKDPNAIFLSFOHLRGKVR 161
||| ||| : : : : : : : : : : : : : : : :

RESULT 13
ABO323
ribonucleoside-diphosphate reductase (EC 1.17.4.1) beta chain [imported] - Yersinia pestis
C;Species: Yersinia pestis
C;Date: 02-Nov-2001 #sequence_revision 02-Nov-2001 #text_change 09-Jul-2004
C;Accession: AB0323
R;Parkhill, J.; Wren, B.W.; Thomson, N.R.; Titball, R.W.; Holden, M.T.G.; Prentice, M.B.; deno-Tarraga, A.M.; Chillingworth, T.; Cronin, A.; Davies, R.M.; Davis, P.; Dougan, G.; Hill, M.; Rutherford, K.; Simmonds, M.; Skelton, J.; Stevens, K.; Whitehead, S.; Barrell, Nature 413, 523-527, 2001
A;Title: Genome sequence of Yersinia pestis, the causative agent of plague.
A;Reference number: AB0001; MUID:21470413; PMID:11586360
A;Accession: AB0323
A>Status: preliminary
A:Molecule type: DNA
A;Residues: 1-323 <KUR>
A;Cross-references: UNIPROT:Q8ZDC8; GB:AL590842; PIDN:CAC92889.1; PID:G15980631; GSPDB:
C;Genetics:
A;Gene: nrdP
C;Superfamily: ribonucleoside-diphosphate reductase beta
C;Keywords: oxidoreductase

Query Match 10.4%; Score 88; DB 2; Length 323;
Best Local Similarity 25.2%; Pred. No. 0.99;
Matches 34; Conservative 20; Mismatches 59; Indels 22; Gaps 5;

Qy 38 NITVPDTKNFYAWKRMVEVGQAQAVEVWQGLLSEAVLRQQALLVNSSQPWEPLQLHVD- 96
||| ||| : : : : : : : : : : : : : : : :
Db 2 NVVKPTRISAINWNKIE-DDKDLEVNN--RLTSNFWLPEKVPLSNDIPSMTALTPEQQ 58
||| ||| : : : : : : : : : : : : : : : :
Qy 97 ---KAVSGLRSLTTLRALGAQ---KEATSPDDAAAPLRTITADTFRKLPFRVYSNFLR 150
:: : : : : : : : : : : : : : : :
Db 59 LATIRVTGTLTTIQTLCAPALIKDAITPBHAIFSNIHFMEAVHARSYSIFSTL-- 116
||| ||| : : : : : : : : : : : : : : : :
Qy 151 GKCLKYTGEACRTGD 165
||| ||| : : : : : : : : : : : : : : : :
Db 117 -----CLTSD 121
||| ||| : : : : : : : : : : : : : : : :

RESULT 14
AE0959
Solute binding receptor protein [imported] - Salmonella enterica subsp. enterica serovar
C;Species: Salmonella enterica subsp. enterica serovar typhi
A;Note: this species has also been called Salmonella typhi
C;Date: 09-Nov-2001 #sequence_revision 09-Nov-2001 #text_change 18-Nov-2002
C;Accession: AE0959
R;Parkhill, J.; Dougan, G.; James, K.D.; Thomson, N.R.; Pickard, D.; Wain, J.; Churcher
th, T.; Connornton, F.; Cronin, A.; Davis, P.; Davies, R.N.; Dowd, L.; White, N.; Farrar
, S.; Moule, S.; O'Gaora, P., Nature 413, 848-852, 2001
A;Authors: Parry, C.; Quail, M.; Rutherford, K.; Simmonds, M.; Skelton, J.; Stevens, K.

GenCore version 5.1.6
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OM protein - protein search, using sw model

Run on: August 23, 2005, 13:52:31 ; Search time 178 Seconds

(without alignments)
474.680 Million cell updates/sec

Title: US-10-706-701-1

Perfect score: 846

Sequence: 1 APPRLICDSRVLYRLLEAK.....SNFLGKLKLYTGACRTGD 165

Scoring table: BLOSUM62

Gapop 10.0 , Gapext 0.5

Searched: 1612378 seqs, 512079187 residues

Total number of hits satisfying chosen parameters: 1612378

Minimum DB seq length: 0

Maximum DB seq length: 2000000000

Post-processing: Minimum Match 0%

Maximum Match 100%

Listing first 45 summaries

Database : UniProt_03.*

1: uniprot_sprot.*

2: uniprot_trembl.*

Pred. No. is the number of results predicted by chance to have a score greater than or equal to the score of the result being printed, and is derived by analysis of the total score distribution.

SUMMARIES

Result No.	Score	Query Match %	Length	ID	Description
1	846	100.0	193	1 EPO_HUMAN	P01588 homo sapien
2	764.5	90.4	192	1 EPO_MACFA	P07865 macaca fasc
3	759.5	89.8	192	1 EPO_MACMU	Q28513 macaca mula
4	723	85.5	192	2 Q867B1	Q867B1 equus cabal
5	706	83.5	192	1 EPO FELCA	P33708 felis silve
6	701	82.9	192	1 EPO RAT	P29676 rattus norv
7	693	81.9	206	2 Q6FWU5	Q6FWU5 canis fami
8	692.5	81.9	192	1 EPO_BOVIN	P48617 bos taurus
9	689	81.4	192	1 EPO_MOUSE	P07321 mus musculu
10	685.5	81.0	194	1 EPO_SHEEP	P33709 ovis aries
11	680.5	80.4	195	2 Q9GKA2	Q9GKA2 oryctolagus
12	680.5	80.4	195	2 Q9GKA3	Q9GKA3 oryctolagus
13	678	80.1	190	1 EPO FIG	P43157 sus scrofa
14	678	80.1	192	2 Q8H8S9	Q8H8S9 spalax gali
15	678	80.1	192	2 Q6H8T0	Q6H8T0 spalax juda
16	678	80.1	192	2 Q6H8T1	Q6H8T1 spalax carm
17	678	80.1	194	2 Q9MYM8	Q9MYM8 sus scrofa
18	674	79.7	192	2 Q8H8T2	Q8H8T2 spalax gola
19	663	78.4	133	2 Q8H288	Q8H288 gorilla gor
20	658	77.8	133	2 Q8H289	Q8H289 pan troglod
21	638	75.4	175	1 EPO_CANFA	P33707 canis fami
22	627	74.1	131	2 Q8H287	Q8H287 pongo pygma
23	607	71.7	133	2 Q8H286	Q8H286 macaca ap
24	554	65.5	133	2 Q8H285	Q8H285 seguinus oe
25	241	28.5	195	2 Q6UAM1	Q6UAM1 tetraodon n
26	238	28.1	182	2 Q6JVT3	Q6JVT3 figu rubrip
27	238	28.1	185	2 Q6JVT2	Q6JVT2 figu rubrip
28	188	22.2	50	2 Q9QV40	Q9QV40 rattus sp.
29	113	13.4	177	2 Q6IYE9	Q6IYE9 gallus gall
30	109	12.9	352	1 TPO_CANFA	P42705 canis fami
31	89	10.5	353	1 TPO_HUMAN	P40225 homo sapien

32	88	10.4	323	2	Q667N4	Q667N4 versinia ps
33	88	10.4	323	2	Q8ZDC8	Q8ZDC8 versinia pe
34	87.5	10.3	346	2	Q8ZDM5	Q8ZDM5 salmonella
35	87.5	10.3	346	2	Q8ZKZ4	Q8ZKZ4 salmonella
36	87.5	10.3	432	2	Q7QDZ2	Q7QDZ2 anopheles g
37	85	10.0	3722	2	P94873	P94873 lysobacter
38	83	9.8	296	2	Q8ZAY4	Q8ZAY4 versinia pe
39	83	9.8	301	2	Q7PKU0	Q7PKU0 anopheles g
40	83	9.8	339	1	MURB_PSEAB	Q9HXM7 pseudomonas
41	82.5	9.8	154	2	Q87AY9	Q87AY9 xylella fas
42	82.5	9.8	558	2	Q7ZUK7	Q7ZUK7 brachydanio
43	82.5	9.8	3033	2	Q9DHD6	Q9DHD6 hepatitis c
44	82	9.7	548	1	CH60_BUCPP	Q8KIX4 buchnera ap
45	82	9.7	815	2	Q9PK31	Q9FK91 arabidopsis

ALIGNMENTS

RESULT 1

ID	EPO_HUMAN	STANDARD;	PRT;	193 AA.
AC	P01588; Q9UDZ0; Q9UEZ5; Q9UHA0;			
DT	21-JUL-1986 (Rel. 01, Created)			
DT	21-JUL-1986 (Rel. 01, Last sequence update)			
DT	25-OCT-2004 (Rel. 45, Last annotation update)			
DE	Erythropoietin precursor (Epoetin).			
GN	Name=EPO;			
OS	Homo sapiens (Human).			
OC	Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;			
OC	Mammalia; Eutheria; Primates; Catarhini; Hominiidae; Homo.			
OX	NCBI_TaxID=9606;			
RN	[1]			
RP	SEQUENCE FROM N.A.			
RX	MEDLINE=85137899; PubMed=3838366;			
RA	Jacobs K., Shoemaker C., Rudersdorf R., Neill S.D., Kaufman R.J.,			
RA	Mufson A., Seehra J., Jones S.S., Hewick R., Fritsch E.F.,			
RA	Kawakita M., Shimizu T., Miyake T.,			
RT	"Isolation and characterization of genomic and cDNA clones of human			
RT	erythropoietin."			
RL	Nature 313:806-810(1985).			
RN	[2]			
RP	SEQUENCE FROM N.A.			
RX	MEDLINE=86067948; PubMed=3865178;			
RA	Lin F.-K., Suggs S., Lin C.-H., Browne J.K., Smalling R., Egrie J.C.,			
RA	Chen K.K., Fox G.M., Martin F., Stabinsky Z., Badrawi S.M., Lai P.-H.,			
RA	Goldwasser E.;			
RT	"Cloning and expression of the human erythropoietin gene."			
RL	Proc. Natl. Acad. Sci. U.S.A. 82:7580-7584(1985).			
RN	[3]			
RP	SEQUENCE FROM N.A.			
RX	MEDLINE=99018118; PubMed=979793;			
RA	Gloeckner G., Scherer S., Schattevoy R., Boright A.P., Weber J.,			
RA	Tsui L.-C., Rosenthal A.;			
RT	"Large-scale sequencing of two regions in human chromosome 7q22:			
RT	analysis of 650 Kb of genomic sequence around the EPO and CUTL1 loci			
RT	reveals 17 genes."			
RL	Genome Res. 8:1060-1073(1998).			
RN	[4]			
RP	SEQUENCE FROM N.A.			
RA	Rupert J.L., Hochachka P.W.;			
RT	"Erythropoietin gene sequence in the Quechua, a high altitude native			
RT	population."			
RL	Submitted (NOV-1999) to the EMBL/GenBank/DBJ databases.			
RN	[5]			
RP	SEQUENCE OF 58-193 FROM N.A., AND VARIANTS HEPATOCELLULAR CARCINOMA			
RP	131-ASN-PHE-132 AND GLN-149.			
RX	MEDLINE=93384593; PubMed=8396923;			
RA	Funakoshi A., Muta H., Baba T., Shimizu S.;			
RT	"Gene expression of mutant erythropoietin in hepatocellular			
RT	carcinoma."			
RL	Biochem. Biophys. Res. Commun. 195:717-722(1993).			
RN	[6]			

QY 1 APRRLICDSRVLYRYLLEAKAEENITTCGAHCSLNENITVPDTKYNFYAWKMEVQQA 60
 Db 28 APRRLICDSRVLYRYLLEAKAEENITTCGAHCSLNENITVPDTKYNFYAWKMEVQQA 87
 QY 61 VEVWQGLALLSEAVLRGOALLVNSOPWEPLQHLVDKAVSGLSLTLRALCAOKEAIS 120
 Db 88 VEVWQGLALLSEAVLRGOALLVNSOPWEPLQHLVDKAVSGLSLTLRALCAOKEAIS 147
 QY 121 PPDASAAAPLRTITADTFKFLFRVYSNFRGLKLYTGACRTGD 165
 Db 148 PPDASAAAPLRTITADTFKFLFRVYSNFRGLKLYTGACRTGD 192

RESULT 2
 EPO_MACFA STANDARD; PRT; 192 AA.
 AC P07865;
 DT 01-AUG-1988 (Rel. 08, Created)
 DT 01-AUG-1988 (Rel. 08, Last sequence update)
 DT 25-OCT-2004 (Rel. 45, Last annotation update)
 DE Erythropoietin precursor.
 GN Name=EPO;
 OS Macaca fascicularis (Crab eating macaque) (Cynomolgus monkey).
 OC Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
 OC Mammalia; Eutheria; Primates; Catarrhini; Cercopitheciidae;
 OC Cercopitheciinae; Macaca.
 OX NCBI_TaxID=9541;
 RN [1]
 RP SEQUENCE FROM N.A.
 RX MEDLINE=87055236; PubMed=2877922; DOI=10.1016/0378-1119(86)90183-6;
 RA Lin F.-K., Lin C.-H., Lai P.-H., Browne J.K., Egrie J.C., Smalling R.,
 RA Fox G.M., Chen K.K., Castro M., Suggs S.;
 RT "Monkey erythropoietin gene: cloning, expression and comparison with
 RT the human erythropoietin gene.";
 RL Gene 44:201-209(1986).
 CC -!- FUNCTION: Erythropoietin is the principal hormone involved in the
 CC regulation of erythrocyte differentiation and the maintenance of a
 CC physiological level of circulating erythrocyte mass.
 CC -!- SUBCELLULAR LOCATION: Secreted.
 CC -!- TISSUE SPECIFICITY: Produced by kidney or liver of adult mammals
 CC and by liver of fetal or neonatal mammals.
 CC -!- SIMILARITY: Belongs to the EPO / TPO family.
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 CC
 CC EMBL; M18189; AAA36841.1; -;
 CC PIR; JQ0173; JQ0173.
 CC HSSP; P01588; 1CN4.
 CC InterPro; IPR009079; 4 helix cytokine.
 CC InterPro; IPR001323; EPO_TPO-
 CC InterPro; IPR003013; Erythroptn.
 CC Pfam; PF00758; EPO_TPO; 1.
 CC PIRSF; PIRSF001951; EPO; 1.
 CC PRINTS; PR00272; ERYTHROPTN.
 CC PROSITE; PS00817; EPO_TPO; 1.
 CC Erythrocyte maturation; Glycoprotein; Hormone; Signal.
 CC SIGNAL 1 27 By similarity.
 CC CHAIN 28 192 Erythropoietin.
 CC DISULFID 34 187 By similarity.
 CC CARBOHYD 51 51 N-linked (GlcNAc...) (By similarity).
 CC CARBOHYD 65 65 N-linked (GlcNAc...) (By similarity).
 CC CARBOHYD 110 110 N-linked (GlcNAc...) (By similarity).
 CC CARBOHYD 152 152 O-linked (GalNAc...) (By similarity).
 CC SEQUENCE 192 AA; 21113 MW; B9A900F442AD4522 CRC64;

Query Match 90.4%; Score 764.5; DB 1; Length 192;
 Best Local Similarity 91.5%; Pred. No. 9.6e-64;
 Matches 151; Conservative 7; Mismatches 6; Indels 1; Gaps 1;

QY 1 APRRLICDSRVLYRYLLEAKAEENITTCGAHCSLNENITVPDTKYNFYAWKMEVQQA 60
 Db 28 APRRLICDSRVLYRYLLEAKAEENITTCGAHCSLNENITVPDTKYNFYAWKMEVQQA 87
 QY 61 VEVWQGLALLSEAVLRGOALLVNSOPWEPLQHLVDKAVSGLSLTLRALCAOKEAIS 120
 Db 88 VEVWQGLALLSEAVLRGOALLVNSOPWEPLQHLVDKAVSGLSLTLRALCAOKEAIS 146
 QY 121 PPDASAAAPLRTITADTFKFLFRVYSNFRGLKLYTGACRTGD 165
 Db 147 LPDASAAAPLRTITADTFKFLFRVYSNFRGLKLYTGACRTGD 191

RESULT 3
 EPO_MACMU STANDARD; PRT; 192 AA.
 AC Q28513;
 DT 01-NOV-1997 (Rel. 35, Created)
 DT 01-NOV-1997 (Rel. 35, Last sequence update)
 DT 25-OCT-2004 (Rel. 45, Last annotation update)
 DE Erythropoietin precursor.
 GN Name=EPO;
 OS Macaca mulatta (Rhesus macaque).
 OC Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
 OC Mammalia; Eutheria; Primates; Catarrhini; Cercopitheciidae;
 OC Cercopitheciinae; Macaca.
 OX NCBI_TaxID=9544;
 RN [1]
 RP SEQUENCE FROM N.A.
 RX MEDLINE=93372347; PubMed=8364201;
 RA Wen D., Boissel J.P.R., Tracy T.E., Gruninger R.H., Mulcahy L.S.,
 RA Czelusniak J., Goodman M., Bunn H.F.;
 RT "Erythropoietin structure-function relationships: high degree of
 RT sequence homology among mammals.";
 RL Blood 82:1507-1516(1993).
 CC -!- FUNCTION: Erythropoietin is the principal hormone involved in the
 CC regulation of erythrocyte differentiation and the maintenance of a
 CC physiological level of circulating erythrocyte mass.
 CC -!- SUBCELLULAR LOCATION: Secreted.
 CC -!- TISSUE SPECIFICITY: Produced by kidney or liver of adult mammals
 CC and by liver of fetal or neonatal mammals.
 CC -!- SIMILARITY: Belongs to the EPO / TPO family.
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 CC
 CC EMBL; L10609; AAA36842.1; -;
 CC PIR; I84613; I84613.
 CC HSSP; P01588; 1CN4.
 CC InterPro; IPR009079; 4 helix cytokine.
 CC InterPro; IPR001323; EPO_TPO-
 CC InterPro; IPR003013; Erythroptn.
 CC Pfam; PF00758; EPO_TPO; 1.
 CC PIRSF; PIRSF001951; EPO; 1.
 CC PRINTS; PR00272; ERYTHROPTN.
 CC PROSITE; PS00817; EPO_TPO; 1.
 CC Erythrocyte maturation; Glycoprotein; Hormone; Signal.
 CC SIGNAL 1 27 By similarity.
 CC CHAIN 28 192 Erythropoietin.
 CC DISULFID 34 187 By similarity.
 CC CARBOHYD 51 51 N-linked (GlcNAc...) (By similarity).
 CC CARBOHYD 65 65 N-linked (GlcNAc...) (By similarity).
 CC SEQUENCE 192 AA; 21113 MW; B9A900F442AD4522 CRC64;

QY 61 VEVWQGLALLSEAVLRGQALLVNSQPMWEPQLQHVDAKAVSLRSLTLLRALGAQKEAIS 120
 DB 87 VEVWQGLALLSEAVLRGQALLVNSQPMWEPQLQHVDAKAVSLRSLTLLRALGAQKEAIS 146

QY 121 PPDAASAAPLRTITADTFRKLVFVYSNFRGLKLYTGACRTGD 165
 DB 147 LPEASAAPLRTITADTFRKLVFVYSNFRGLKLYTGACRTGD 191

RESULT 6
 ID EPO RAT STANDARD; PRT; 192 AA.
 AC P29676; P70504;
 DT 01-APR-1993 (Rel. 25, Created)
 DT 01-APR-1993 (Rel. 25, Last sequence update)
 DT 25-OCT-2004 (Rel. 45, Last annotation update)
 DE Erythropoietin precursor.
 GN Name=Epo;
 OS Rattus norvegicus (Rat).
 OC Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
 OC Mammalia; Eutheria; Rodentia; Sciurognathi; Muridae; Murinae; Rattus.
 OX NCBI_TaxID=10116;
 RN [1]
 RP SEQUENCE FROM N.A.
 RC STRAIN=Wistar; TISSUE=Kidney;
 RX MEDLINE=93042015; PubMed=8364201;
 RA Nagao M., Suga H., Okano M., Masuda S., Narita H., Ikura K.,
 RA Sasaki R.;
 RT "Nucleotide sequence of rat erythropoietin."
 RL Biochim. Biophys. Acta 1171:99-102(1992).
 [2]
 RP SEQUENCE OF 4-192 FROM N.A.
 RC STRAIN=Sprague-Dawley; TISSUE=Kidney;
 RX MEDLINE=93372347; PubMed=8364201;
 RA Wen D., Boissel J.P.R., Tracy T.E., Mulcahy L.S., Czelusniak J.,
 RA Goodman M., Bunn H.F.;
 RT "Erythropoietin structure-function relationships: high degree of
 sequence homology among mammals."
 RL Blood 82:1507-1516(1993).
 CC -!- FUNCTION: Erythropoietin is the principal hormone involved in the
 regulation of erythrocyte differentiation and the maintenance of a
 physiological level of circulating erythrocyte mass.
 CC -!- SUBCELLULAR LOCATION: Secreted.
 CC -!- TISSUE SPECIFICITY: Produced by kidney or liver of adult mammals
 and by liver of fetal or neonatal mammals.
 CC -!- SIMILARITY: Belongs to the EPO / TPO family.
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 CC
 DR EMBL; D10763; BAA01593.1; -;
 DR EMBL; L10608; AAA41126.1; -;
 DR PIR; S28148; S28148.
 DR HSSP; P01588; 1CM4.
 DR RGD; 2559; Epo.
 DR InterPro; IPR009079; 4_helix_cytokine.
 DR InterPro; IPR001323; EPO_TPO.
 DR InterPro; IPR003013; Erythroptn.
 DR Pfam; PF00758; EPO_TPO; 1.
 DR PIRSP; PIRSF001951; EPO; 1.
 DR PRINTS; PR00272; ERYTHROPTN.
 DR PROSITE; PS00817; EPO_TPO; 1.
 DR Erythrocyte maturation; Glycoprotein; Hormone; Signal.
 FT SIGNAL 1 26 By similarity.
 FT CHAIN 27 192 Erythropoietin.
 FT DISULFID 33 187 By similarity.
 FT CARBOHYD 50 50 N-linked (GlcNAc...) (By similarity).
 FT CARBOHYD 64 64 N-linked (GlcNAc...) (By similarity).

FT CARBOHYD 109 109 N-linked (GlcNAc...) (By similarity).
 SQ SEQUENCE 192 AA; 21286 MW; 3EA632737ED2443 CRC64;

Query Match 82.9%; Score 701; DB 1; Length 192;
 Best Local Similarity 82.4%; Pred. No. 9e-58;
 Matches 136; Conservative 13; Mismatches 16; Indels 0; Gaps 0;

QY 1 APPRLICDSRVLEKAEENITTCGAECSLNENITVPTKYNFYAWKMEVGOQA 60
 DB 27 APPRLICDSRVLEKAEENITTCGAECSLNENITVPTKYNFYAWKMEVGOQA 86

QY 61 VEVWQGLALLSEAVLRGQALLVNSQPMWEPQLQHVDAKAVSLRSLTLLRALGAQKEAIS 120
 DB 87 VEVWQGLALLSEAVLRGQALLVNSQPMWEPQLQHVDAKAVSLRSLTLLRALGAQKEAIS 146

QY 121 PPDAASAAPLRTITADTFRKLVFVYSNFRGLKLYTGACRTGD 165
 DB 147 PPDAASAAPLRTITADTFRKLVFVYSNFRGLKLYTGACRTGD 191

RESULT 7
 ID Q6PWU5 PRELIMINARY; PRT; 206 AA.
 AC Q6PWU5;
 DT 05-JUL-2004 (TREMBlrel. 27, Created)
 DT 05-JUL-2004 (TREMBlrel. 27, Last sequence update)
 DE Erythropoietin.
 OS Canis familiaris (Dog).
 OC Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
 OC Mammalia; Eutheria; Carnivora; Fissipedia; Canidae; Canis.
 OX NCBI_TaxID=9615;
 RN [1]
 RP SEQUENCE FROM N.A.
 RC TISSUE=Kidney;
 RA Souza D.S., Vicentim D.L., Costa F.F., Saad S.T.O.;
 RL Submitted (MAR-2004) to the EMBL/GenBank/DBJ databases.
 DR EMBL; AY572971; AAS77874.1; -;
 DR GO; GO:0005576; C:extracellular; IEA.
 DR GO; GO:0005128; P:erythropoietin receptor binding; IEA.
 DR GO; GO:0005179; P:hormone activity; IEA.
 DR InterPro; IPR009079; 4_helix_cytokine.
 DR InterPro; IPR001323; EPO_TPO.
 DR Pfam; PF00758; EPO_TPO; 1.
 DR PRINTS; PR00272; ERYTHROPTN.
 DR PROSITE; PS00817; EPO_TPO; 1.
 SQ SEQUENCE 206 AA; 22666 MW; 1EBC64A02CE4F5B0 CRC64;

Query Match 81.9%; Score 693; DB 2; Length 206;
 Best Local Similarity 81.2%; Pred. No. 5.5e-57;
 Matches 134; Conservative 13; Mismatches 18; Indels 0; Gaps 0;

QY 1 APPRLICDSRVLEKAEENITTCGAECSLNENITVPTKYNFYAWKMEVGOQA 60
 DB 41 APPRLICDSRVLEKAEENITTCGAECSLNENITVPTKYNFYAWKMEVGOQA 100

QY 61 VEVWQGLALLSEAVLRGQALLVNSQPMWEPQLQHVDAKAVSLRSLTLLRALGAQKEAIS 120
 DB 101 VEVWQGLALLSEAVLRGQALLVNSQPMWEPQLQHVDAKAVSLRSLTLLRALGAQKEAIS 160

QY 121 PPDAASAAPLRTITADTFRKLVFVYSNFRGLKLYTGACRTGD 165
 DB 161 LPEASAAPLRTITADTFRKLVFVYSNFRGLKLYTGACRTGD 205

RESULT 8
 ID EPO BOVIN STANDARD; PRT; 192 AA.
 AC P48617;
 DT 01-FEB-1996 (Rel. 33, Created)
 DT 01-FEB-1996 (Rel. 33, Last sequence update)
 DT 25-OCT-2004 (Rel. 45, Last annotation update)

KW Erythrocyte maturation; Glycoprotein; Hormone; Signal.
 FT SIGNAL 1 26
 FT CHAIN 27 192 Erythropoietin.
 FT DISULFID 33 187 By similarity.
 FT CARBOHYD 50 50 N-linked (GlcNAc...) (By similarity).
 FT CARBOHYD 64 64 N-linked (GlcNAc...) (By similarity).
 FT CARBOHYD 109 109 N-linked (GlcNAc...) (By similarity).
 SQ SEQUENCE 192 AA; 21365 MW; 65F94E214E0DEP2E CRC64;

Query Match 81.4%; Score 689; DB 1; Length 192;
 Best Local Similarity 80.0%; Pred. No. 1.2e-56;
 Matches 132; Conservative 14; Mismatches 19; Indels 0; Gaps 0;

QY 1 APPRLICDSRVLELYLEAKEAENITTCAGHCSLNENITVPTKYNFYAWKMEVGOQA 60
 DB 27 APPRLICDSRVLELYLEAKEAENITTCAGHCSLNENITVPTKYNFYAWKMEVGOQA 86
 QY 61 VEWQGLALLSEAVLRGOALLVNSSQPWEPLQHLVDKAVSGLSLTLLRALGAQKEAIS 120
 DB 87 IEVWQGLSLSRAILQAALLANSSQPETQLQHLIDKAIKSLSLTLLRALGAQKEAIS 146
 QY 121 PPDASAAPLRITATDTFKLFRVYNSFLRGKLYTGEACRTGD 165
 DB 147 PPDTPPAFLRTLTVDTFCKLFRVYANFLRGKLYTGEVCRGD 191

RESULT 10
 EPO_SHEEP STANDARD; PRT; 194 AA.
 AC P33709; Q28572;
 DT 01-FEB-1994 (Rel. 28, Created)
 DT 01-FEB-1994 (Rel. 28, Last sequence update)
 DT 25-OCT-2004 (Rel. 45, Last annotation update)
 DE Erythropoietin precursor.
 GN Name=EPO;
 OS Ovis aries (Sheep).
 OC Eukaryota; Metazoa; Chordata; Vertebrata; Euteleostomi;
 OC Mammalia; Eutheria; Cetartiodactyla; Ruminantia; Pecora; Bovidae;
 OC Caprinae; Ovis.
 OX NCBI_TaxID=9940;
 RN [1]
 RP SEQUENCE FROM N.A.
 RC TISSUE=Kidney;
 RX MEDLINE=93351736; PubMed=8349021; DOI=10.1016/0303-7207(93)90113-X;
 RA Fu P., Evans B., Lim G.B., Moritz K., Wintour M.E.;
 RT "The sheep erythropoietin gene: molecular cloning and effect of
 RT hemorrhage on plasma erythropoietin and renal/liver messenger RNA in
 RL adult sheep";
 RL Mol. Cell. Endocrinol. 93:107-116(1993).
 RN [2]
 RP SEQUENCE OF 4-194 FROM N.A.
 RC TISSUE=Kidney;
 RX MEDLINE=93372347; PubMed=8364201;
 RA Wen D., Boessel J.P.R., Tracy T.E., Gruninger R.H., Mulcahy L.S.,
 RA Czelusniak J., Goodman M., Bunn H.P.;
 RT "Erythropoietin structure-function relationships: high degree of
 RT sequence homology among mammals.";
 RL Blood 82:1507-1516(1993).
 CC -!- FUNCTION: Erythropoietin is the principal hormone involved in the
 CC regulation of erythrocyte differentiation and the maintenance of a
 CC physiological level of circulating erythrocyte mass.
 CC -!- SUBCELLULAR LOCATION: Secreted.
 CC -!- TISSUE SPECIFICITY: Produced by kidney or liver of adult mammals
 CC and by liver of fetal or neonatal mammals.
 CC -!- SIMILARITY: Belongs to the EPO / TPO family.
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CC EMBL; Z24681; CAA80848.1; -
 CC EMBL; L10610; AAA31518.1; -
 CC PIR; I46401; I46401.
 CC HSP; P01588; ICN4.
 CC InterPro; IPR009079; 4 helix cytokine.
 CC InterPro; IPR001323; EPO TPO.
 CC InterPro; IPR003013; Erythroptn.
 CC Pfam; PF00758; EPO TPO; 1.
 CC PIRSF; PIRSF001951; EPO; 1.
 CC PRINTS; PR00272; ERYTHROPTN.
 CC PROSITE; PS00817; EPO TPO; 1.
 KW Erythrocyte maturation; Glycoprotein; Hormone; Signal.
 FT SIGNAL 1 27 By similarity.
 FT CHAIN 28 194 Erythropoietin.
 FT DISULFID 34 189 By similarity.
 FT DISULFID 56 60 By similarity.
 FT CARBOHYD 51 51 N-linked (GlcNAc...) (Potential).
 FT CARBOHYD 65 65 N-linked (GlcNAc...) (Potential).
 FT CARBOHYD 110 110 N-linked (GlcNAc...) (Potential).
 FT CONFLICT 16 16 F -> L (in Ref. 2).
 FT CONFLICT 108 108 L -> P (in Ref. 2).
 SQ SEQUENCE 194 AA; 21335 MW; C025A80528131A9 CRC64;

Query Match 81.0%; Score 685.5; DB 1; Length 194;
 Best Local Similarity 81.9%; Pred. No. 2.6e-56;
 Matches 136; Conservative 9; Mismatches 20; Indels 1; Gaps 1;

QY 1 APPRLICDSRVLELYLEAKEAENITTCAGHCSLNENITVPTKYNFYAWKMEVGOQA 60
 DB 28 APPRLICDSRVLELYLEAKEAENITTCAGHCSLNENITVPTKYNFYAWKMEVGOQA 87
 QY 61 VEWQGLALLSEAVLRGOALLVNSSQPWEPLQHLVDKAVSGLSLTLLRALGAQKEAIS 120
 DB 88 LEVWQGLALLSEAVLRGOALLVNSSQPWEPLQHLVDKAVSGLSLTLLRALGAQKEAIS 147
 QY 121 PPDAA-SAAPLRITATDTFKLFRVYNSFLRGKLYTGEACRTGD 165
 DB 148 LPDAPSAAPLRITATDTFKLFRVYNSFLRGKLYTGEACRTGD 193

RESULT 11
 O9GKA2 PRELIMINARY; PRT; 195 AA.
 ID O9GKA2
 AC O9GKA2;
 DT 01-MAR-2001 (TrEMBLrel. 16, Created)
 DT 01-MAR-2001 (TrEMBLrel. 16, Last sequence update)
 DT 01-MAR-2004 (TrEMBLrel. 26, Last annotation update)
 DE Erythropoietin.
 OS Oryctolagus cuniculus (Rabbit).
 OC Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
 OC Mammalia; Eutheria; Lagomorpha; Leporidae; Oryctolagus.
 OX NCBI_TaxID=9986;
 RN [1]
 RP SEQUENCE FROM N.A.
 RX MEDLINE=21290682; PubMed=11396976; DOI=10.1006/bbrc.2001.5028;
 RA Vilalta A., Wu D., Margalith M., Hobart P.;
 RT "Rabbit EPO gene and cDNA: expression of rabbit EPO after
 RT intramuscular injection of pDNA.";
 RL Biochem. Biophys. Res. Commun. 284:823-827(2001).
 DR EMBL; AF290944; AAG36962.1; -
 DR HSP; P01588; ICN4.
 DR GO; GO:0005576; C:extracellular; IEA.
 DR GO; GO:0005128; F:erythropoietin receptor binding; IEA.
 DR GO; GO:0005179; F:hormone activity; IEA.
 DR InterPro; IPR009079; 4 helix cytokine.
 DR InterPro; IPR001323; EPO TPO.
 DR InterPro; IPR003013; Erythroptn.
 DR Pfam; PF00758; EPO TPO; 1.
 DR PIRSF; PIRSF001951; EPO; 1.
 DR PRINTS; PR00272; ERYTHROPTN.
 DR PROSITE; PS00817; EPO TPO; 1.
 SQ SEQUENCE 195 AA; 21025 MW; 1F1DC7F403A303EC CRC64;

Q6H8S9
ID Q6H8S9 PRELIMINARY; PRT; 192 AA.
AC Q6H8S9;
DT 05-JUL-2004 (TREMBlrel. 27, Created)
DT 05-JUL-2004 (TREMBlrel. 27, Last sequence update)
DT 05-JUL-2004 (TREMBlrel. 27, Last annotation update)
DE Erythropoietin precursor.
GN Name=epo;
OS Spalax galili.
OC Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
OC Mammalia; Eutheria; Rodentia; Sciurognathi; Muridae; Spalacinae;
OC Spalax.
OX NCBI_TaxID=164323;
RN [1] TAXID=164323;
RP SEQUENCE FROM N.A.
RC TISSUE=Liver;
RA Shams I., Avioli A., Nevo E.;
RT "Hypoxic stress tolerance of the blind subterranean mole rat: Expression of erythropoietin and hypoxia-inducible factor-1a.";
RL Nucleic Acids Res. 0:0-0(2004).
RN [2]
RP SEQUENCE FROM N.A.
RC TISSUE=Liver;
RX PubMed=15210955; DOI=10.1073/pnas.0403540101;
RA Shams I., Avioli A., Eviatar N.;
RT "Hypoxic stress tolerance of the blind subterranean mole rat: expression of erythropoietin and hypoxia-inducible factor 1 alpha.";
RL Proc. Natl. Acad. Sci. U.S.A. 101:9698-9703(2004).
DR EMBL; AJ715795; CAG29400.1; -;
DR GO; GO:0005576; C:extracellular; IEA.
DR GO; GO:0005128; F:erythropoietin receptor binding; IEA.
DR GO; GO:0005179; F:hormone activity; IEA.
DR InterPro; IPR009079; 4_helix_cytokine.
DR InterPro; IPR001323; EPO_TPO.
DR Pfam; PF00758; EPO_TPO; 1.
DR PRINTS; PR00272; ERYTHROPTN.
DR PROSITE; PS00817; EPO_TPO; 1.
KW Signal.
FT SIGNAL.
FT CHAIN
SQ SEQUENCE 192 AA; 21372 MW; 72FCA94DB8C5AAB5 CRC64;
Query Match 80.1%; Score 678; DB 2; Length 192;
Best Local Similarity 80.6%; Pred. No. 1.3e-55;
Matches 133; Conservative 8; Mismatches 24; Indels 0; Gaps 0;
QY 1 APPRLICDSRVLYRLLLEAKEAENITTCAGHCNENITVPDTKYNFYAKRMVEGQQA 60
Db 27 APPRLICDSRVLYRLLLEAKEAENITTCAGHCNENITVPDTKYNFYAKRMVEGQQA 86
QY 61 VEVWQGLALLSEAVLRGQALLVNSQWPPEQLQHVDAKAVSGRLSLTLLRALGAQKEAIS 120
Db 87 VEVWQGLSLLPEAILRAQAVLANSSQPSSEMLQLHVDKAIISGLRSLTLLRALGAQKEAIS 146
QY 121 PDAAASAAPLRITITADTFKLPFRVYSNPLRGKLYTGACRTGD 165
Db 147 PPDTTQVPLRRFTVDTCKLFRIYSNPLRGKLYTGACRRGD 191
RESULT 15
Q6H8T0 PRELIMINARY; PRT; 192 AA.
ID Q6H8T0
AC Q6H8T0;
DT 05-JUL-2004 (TREMBlrel. 27, Created)
DT 05-JUL-2004 (TREMBlrel. 27, Last sequence update)
DT 05-JUL-2004 (TREMBlrel. 27, Last annotation update)
DE Erythropoietin precursor.
GN Name=epo;
OS Spalax judaei (Blind subterranean mole rat).
OC Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
OC Mammalia; Eutheria; Rodentia; Sciurognathi; Muridae; Spalacinae;
OC Spalax.

OX NCBI_TaxID=134510;
RN [1] TAXID=134510;
RP SEQUENCE FROM N.A.
RC TISSUE=Liver;
RA Shams I., Avioli A., Nevo E.;
RT "Hypoxic stress tolerance of the subterranean mole rat: Expression of erythropoietin and hypoxia-inducible factor-1a.";
RL Nucleic Acids Res. 0:0-0(2004).
RN [2]
RP SEQUENCE FROM N.A.
RC TISSUE=Liver;
RX PubMed=15210955; DOI=10.1073/pnas.0403540101;
RA Shams I., Avioli A., Eviatar N.;
RT "Hypoxic stress tolerance of the blind subterranean mole rat: expression of erythropoietin and hypoxia-inducible factor 1 alpha.";
RL Proc. Natl. Acad. Sci. U.S.A. 101:9698-9703(2004).
DR EMBL; AJ715794; CAG29399.1; -;
DR GO; GO:0005576; C:extracellular; IEA.
DR GO; GO:0005128; F:erythropoietin receptor binding; IEA.
DR GO; GO:0005179; F:hormone activity; IEA.
DR InterPro; IPR009079; 4_helix_cytokine.
DR InterPro; IPR001323; EPO_TPO.
DR Pfam; PF00758; EPO_TPO; 1.
DR PRINTS; PR00272; ERYTHROPTN.
DR PROSITE; PS00817; EPO_TPO; 1.
KW Signal.
FT SIGNAL.
FT CHAIN
SQ SEQUENCE 192 AA; 21372 MW; 72FCA94DB8C5AAB5 CRC64;
Query Match 80.1%; Score 678; DB 2; Length 192;
Best Local Similarity 80.6%; Pred. No. 1.3e-55;
Matches 133; Conservative 8; Mismatches 24; Indels 0; Gaps 0;
QY 1 APPRLICDSRVLYRLLLEAKEAENITTCAGHCNENITVPDTKYNFYAKRMVEGQQA 60
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QY 61 VEVWQGLALLSEAVLRGQALLVNSQWPPEQLQHVDAKAVSGRLSLTLLRALGAQKEAIS 120
Db 87 VEVWQGLSLLPEAILRAQAVLANSSQPSSEMLQLHVDKAIISGLRSLTLLRALGAQKEAIS 146
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Db 147 PPDTTQVPLRRFTVDTCKLFRIYSNPLRGKLYTGACRRGD 191
Search completed: August 23, 2005, 13:55:39
Job time : 181 secs


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; Sequence 2, Application US/09604871
; Patent No. 6340742
; GENERAL INFORMATION:
; APPLICANT: Burg, Josef
; APPLICANT: Hilger, Bernd
; APPLICANT: Josel, Hans-Peter
; TITLE OF INVENTION: ERYTHROPOIETIN CONJUGATES
; FILE REFERENCE: 1098 nonprovisional
; CURRENT APPLICATION NUMBER: US/09/604,871
; CURRENT FILING DATE: 2000-06-28
; PRIOR APPLICATION NUMBER: 60/151,454
; PRIOR FILING DATE: 1999-08-30
; PRIOR APPLICATION NUMBER: 60/147,452
; PRIOR FILING DATE: 1999-08-05
; PRIOR APPLICATION NUMBER: 60/142,243
; PRIOR FILING DATE: 1999-07-02
; NUMBER OF SEQ ID NOS: 3
; SOFTWARE: Patent in Ver. 2.1
; SEQ ID NO 2
; LENGTH: 166
; TYPE: PRT
; ORGANISM: Homo sapiens
US-09-604-871-2

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Best Local Similarity 100.0%; Pred. No. 1.5e-99;
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; Sequence 2, Application US/09604938
; Patent No. 6583272
; GENERAL INFORMATION:
; APPLICANT: Bailon, Pascal
; TITLE OF INVENTION: ERYTHROPOIETIN CONJUGATES
; FILE REFERENCE: 1097 nonprovisional
; CURRENT APPLICATION NUMBER: US/09/604,938
; CURRENT FILING DATE: 2000-06-27
; PRIOR APPLICATION NUMBER: 60/166,151
; PRIOR FILING DATE: 1999-11-17
; PRIOR APPLICATION NUMBER: 60/151,548
; PRIOR FILING DATE: 1999-08-13
; PRIOR APPLICATION NUMBER: 60/150,225
; PRIOR FILING DATE: 1999-08-23
; PRIOR APPLICATION NUMBER: 60/142,254
; PRIOR FILING DATE: 1999-07-02
; NUMBER OF SEQ ID NOS: 3
; SOFTWARE: Patent in Ver. 2.1
; SEQ ID NO 2
; LENGTH: 166
; TYPE: PRT
; ORGANISM: Homo sapiens
US-09-604-938-2

Query Match      100.0%; Score 846; DB 4; Length 166;
Best Local Similarity 100.0%; Pred. No. 1.5e-99;
Matches 165; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

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DB 61 VEVWQGLALLSEAVLRGQALLVNSSQPWEPLQLHVDKAVSGLSRLTLLRALGAQKEAIS 120
QY 121 PPDAASAAPLRTITADTRFKLFRVYSNFRGKGLKLYTGEACRTGD 165
DB 121 PPDAASAAPLRTITADTRFKLFRVYSNFRGKGLKLYTGEACRTGD 165

RESULT 7
US-09-462-941-2
; Sequence 2, Application US/09462941
; Patent No. 6608183
; GENERAL INFORMATION:
; APPLICANT: Cox III, George N
; APPLICANT: Bolder Biotechnology, Inc.
; TITLE OF INVENTION: Derivatives of Growth Hormone and Related Proteins
; FILE REFERENCE: 4152-1-PUS
; CURRENT APPLICATION NUMBER: US/09/462,941
; CURRENT FILING DATE: 2000-01-14
; PRIOR APPLICATION NUMBER: 60/052,516
; PRIOR FILING DATE: 1997-07-14
; NUMBER OF SEQ ID NOS: 41
; SOFTWARE: Patent in Ver. 2.0
; SEQ ID NO 2
; LENGTH: 166
; TYPE: PRT
; ORGANISM: Homo sapiens
US-09-462-941-2

Query Match      100.0%; Score 846; DB 4; Length 166;
Best Local Similarity 100.0%; Pred. No. 1.5e-99;
Matches 165; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

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RESULT 8
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; Sequence 37, Application PC/TUS9404361
; GENERAL INFORMATION:
; APPLICANT: Brigham and Women's Hospital
; APPLICANT: 75 Francis Street
; APPLICANT: Boston, MA 02115
; APPLICANT: Bunn, H. Franklin
; APPLICANT: Wen, Danyi
; APPLICANT: Showers, Mark O.
; TITLE OF INVENTION: Erythropoietin Muteins With Enhanced
; TITLE OF INVENTION: Activity
; NUMBER OF SEQUENCES: 59
; CORRESPONDENCE ADDRESS:
; ADDRESSEE: Sterne, Kessler, Goldstein & Fox
; STREET: 1100 New York Avenue, Suite 600
; CITY: Washington
; STATE: D.C.
; COUNTRY: U.S.A.
; ZIP: 20005-3934
; COMPUTER READABLE FORM:
; MEDIUM TYPE: Floppy disk
; COMPUTER: IBM PC compatible
; OPERATING SYSTEM: PC-DOS/MS-DOS
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RESULT 11

US-09-552-265B-4
; Sequence 4, Application US/09552265B
; Patent No. 6555343
; GENERAL INFORMATION:
; APPLICANT: DeSavage, Frederick
; APPLICANT: Henner, Dennis, J.
; TITLE OF INVENTION: No. 6555343el chimpanzee erythropoietin (chepo)
; FILE REFERENCE: polypeptides and nucleic acids encoding the same
; CURRENT APPLICATION NUMBER: US/09/552,265B
; PRIOR FILING DATE: 2000-04-19
; PRIOR APPLICATION NUMBER: US 09/307307
; PRIOR FILING DATE: 1999-05-17
; NUMBER OF SEQ ID NOS: 49
; SOFTWARE: FastSeq for Windows Version 4.0
; SEQ ID NO 4
; LENGTH: 193
; TYPE: PRT
; ORGANISM: Homo sapiens
US-09-552-265B-4

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US-09-813-775C-4
; Sequence 4, Application US/09813775C
; Patent No. 6831060
; GENERAL INFORMATION:
; APPLICANT: DeSavage, Frederick
; APPLICANT: Henner, Dennis, J.
; TITLE OF INVENTION: No. 6831060el chimpanzee erythropoietin
; FILE REFERENCE: polypeptides and nucleic acids encoding the same
; CURRENT APPLICATION NUMBER: US/09/813,775C
; PRIOR FILING DATE: 1999-05-07
; PRIOR APPLICATION NUMBER: US 09/307307
; PRIOR FILING DATE: 1999-05-07
; PRIOR APPLICATION NUMBER: US 09/552265
; PRIOR FILING DATE: 2000-04-19
; NUMBER OF SEQ ID NOS: 52
; SOFTWARE: FastSeq for Windows Version 4.0
; SEQ ID NO 4
; LENGTH: 193
; TYPE: PRT
; ORGANISM: Homo sapiens
US-09-813-775C-4

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Db 148 PPDAASAAPLRTITADTFRKLFRVYSNFRGLKLYTGEACRTGD 192

RESULT 13

US-09-554-451-8
; Sequence 8, Application US/09554451
; Patent No. 6680207
; GENERAL INFORMATION:
; APPLICANT: Jonathan Paul MURPHY
; APPLICANT: Anthony ATKINSON
; TITLE OF INVENTION: Detection of Molecules in Samples
; NUMBER OF SEQUENCES: 9
; CORRESPONDENCE ADDRESS:
; ADDRESS: Pillsbury Winthrop, L.L.P.
; STREET: 1100 New York Ave., N.W.
; CITY: Washington
; STATE: D.C.
; COUNTRY: U.S.A.
; ZIP: 20005
; COMPUTER READABLE FORM:
; MEDIUM TYPE: Diskette
; COMPUTER: IBM PC compatible
; OPERATING SYSTEM: PC-DOS/MS-DOS
; SOFTWARE: MS Word
; CURRENT APPLICATION DATA:
; APPLICATION NUMBER: US/09/554,451
; FILING DATE: 15-May-2000
; CLASSIFICATION: <Unknown>
; PRIOR APPLICATION DATA:
; APPLICATION NUMBER: PCT/GB98/03449
; FILING DATE: No. 6680207ember 16, 1998
; APPLICATION NUMBER: GB 9723955.2
; FILING DATE: No. 6680207ember 14, 1997
; INFORMATION FOR SEQ ID NO: 8:
; SEQUENCE CHARACTERISTICS:
; LENGTH: 165 amino acids
; TYPE: amino acid
; STRANDEDNESS: single
; TOPOLOGY: linear
; SEQUENCE DESCRIPTION: SEQ ID NO: 8:
US-09-554-451-8

Query Match 99.6%; Score 843; DB 4; Length 165;
Best Local Similarity 99.4%; Pred. No. 3.5e-99;
Matches 164; Conservative 1; Mismatches 0; Indels 0; Gaps 0;
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GenCore version 5.1.6
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Run on: August 23, 2005, 14:17:43 ; Search time 64 Seconds

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Title: US-10-706-701-1

Perfect score: 846

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Total number of hits satisfying chosen parameters: 71

Minimum DB seq length: 0

Maximum DB seq length: 2000000000

Post-processing: Minimum Match 100%

Maximum Match 100%

Listing first 500 summaries

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Pred. No. is the number of results predicted by chance to have a score greater than or equal to the score of the result being printed, and is derived by analysis of the total score distribution.

SUMMARIES

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4	846	100.0	165	14	US-10-241-356-1
5	846	100.0	165	14	US-10-293-551-1
6	846	100.0	165	15	US-10-411-037-3
7	846	100.0	165	15	US-10-411-026-73
8	846	100.0	165	15	US-10-410-962-73
9	846	100.0	165	15	US-10-411-049-73
10	846	100.0	165	16	US-10-634-477-1
11	846	100.0	165	16	US-10-410-930-73

ALIGNMENTS

RESULT 1

US-09-853-731-1

; Sequence 1, Application US/09853731

; Patent No. US20020037841A1

; GENERAL INFORMATION:

; APPLICANT: Papadimitriou, Apollon

; TITLE OF INVENTION: Erythropoietin Composition

; FILE REFERENCE: 20619 US

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24	846	100.0	166	14	US-10-400-708-2	Sequence 2, Appl
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31	846	100.0	166	16	US-10-468-436-133	Sequence 133, App
32	846	100.0	166	16	US-10-773-654-2	Sequence 2, Appl
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41	846	100.0	174	13	US-10-014-363-5	Sequence 5, Appl
42	846	100.0	193	10	US-09-813-775C-4	Sequence 4, Appl
43	846	100.0	193	14	US-10-113-824-2	Sequence 2, Appl
44	846	100.0	193	16	US-10-612-665-10	Sequence 10, Appl
45	846	100.0	193	16	US-10-612-665-22	Sequence 22, Appl
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47	846	100.0	193	16	US-10-676-694-10	Sequence 10, Appl
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49	846	100.0	193	16	US-10-676-694-112	Sequence 112, App
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; Sequence 1, Application US/10293551
; Publication No. US20030120045A1
; GENERAL INFORMATION:
; APPLICANT: Bailon, Pascal
; TITLE OF INVENTION: ERYTHROPOIETIN CONJUGATES
; FILE REFERENCE: 1097 nonprovisional
; CURRENT APPLICATION NUMBER: US/10/293,551
; CURRENT FILING DATE: 2002-11-14
; PRIOR APPLICATION NUMBER: US/09/604,938
; PRIOR FILING DATE: 2000-06-27
; PRIOR APPLICATION NUMBER: 60/166,151
; PRIOR FILING DATE: 1999-11-17
; PRIOR APPLICATION NUMBER: 60/151,548
; PRIOR FILING DATE: 1999-08-13
; PRIOR APPLICATION NUMBER: 60/150,225
; PRIOR FILING DATE: 1999-08-23
; PRIOR APPLICATION NUMBER: 60/142,254
; PRIOR FILING DATE: 1999-07-02
; NUMBER OF SEQ ID NOS: 3
; SOFTWARE: PatentIn Ver. 2.1
; SEQ ID NO 1
; LENGTH: 165
; TYPE: PRT
; ORGANISM: Homo sapiens
US-10-293-551-1

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Matches 165; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

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RESULT 6
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; Sequence 73, Application US/10411037
; Publication No. US20040043446A1
; GENERAL INFORMATION:
; APPLICANT: Neose Technologies, Inc.
; APPLICANT: DeFrees, Shawn
; APPLICANT: Zopf, David
; APPLICANT: Bayer, Robert
; APPLICANT: Hakes, David
; APPLICANT: Chen, Xi
; APPLICANT: Bows, Caryn
; TITLE OF INVENTION: ALPHA GALACTOSIDASE A: REMODELING AND GLYCOCONJUGATION OF ALPHA
; FILE REFERENCE: 040853-01-5082
; CURRENT APPLICATION NUMBER: US/10/411,037
; CURRENT FILING DATE: 2003-04-09
; PRIOR APPLICATION NUMBER: US 60/328,523
; PRIOR FILING DATE: 2001-10-10
; PRIOR APPLICATION NUMBER: US 60/344,692
; PRIOR FILING DATE: 2001-10-19
; PRIOR APPLICATION NUMBER: US 60/387,292
; PRIOR FILING DATE: 2002-06-07
; PRIOR APPLICATION NUMBER: US 60/391,777
; PRIOR FILING DATE: 2002-06-25
; PRIOR APPLICATION NUMBER: US 60/396,594
; PRIOR FILING DATE: 2002-07-17
; PRIOR APPLICATION NUMBER: US 60/404,249
; PRIOR FILING DATE: 2002-08-16
; PRIOR APPLICATION NUMBER: US 60/407,527
; NUMBER OF SEQ ID NOS: 3
; SOFTWARE: PatentIn version 3.2
; SEQ ID NO 73
; LENGTH: 165
; TYPE: PRT
; ORGANISM: Homo sapiens
US-10-411-026-73

Query Match      100.0%; Score 846; DB 15; Length 165;
Best Local Similarity 100.0%; Pred. No. 1.4e-85;
Matches 165; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

QY 1 APPRLICDSRVLYRLLEAKEAENITTCGAHCSSLNENITVPDTKYNFYAWKMEVGGQA 60
DB 1 APPRLICDSRVLYRLLEAKEAENITTCGAHCSSLNENITVPDTKYNFYAWKMEVGGQA 60
QY 61 VEVWQGLALLSEAVLRGQALLVNSSQPWEPLQLHVDKAVSGRLSLTTLRALGAQKEAIS 120
DB 61 VEVWQGLALLSEAVLRGQALLVNSSQPWEPLQLHVDKAVSGRLSLTTLRALGAQKEAIS 120
QY 121 PPDAASAAPLRTITADTFKFLFRVYSNFLRGKLYTGACRTGD 165
DB 121 PPDAASAAPLRTITADTFKFLFRVYSNFLRGKLYTGACRTGD 165

RESULT 7
US-10-411-026-73
; Sequence 73, Application US/10411026
; Publication No. US20040063911A1
; GENERAL INFORMATION:
; APPLICANT: Neose Technologies, Inc.
; APPLICANT: DeFrees, Shawn
; APPLICANT: Zopf, David
; APPLICANT: Bayer, Robert
; APPLICANT: Hakes, David
; APPLICANT: Chen, Xi
; TITLE OF INVENTION: PROTEIN REMODELING METHODS AND PROTEINS/PEPTIDES PRODUCED BY THE
; FILE REFERENCE: 040853-01-5053
; CURRENT APPLICATION NUMBER: US/10/411,026
; CURRENT FILING DATE: 2003-04-09
; PRIOR APPLICATION NUMBER: US 60/328,523
; PRIOR FILING DATE: 2001-10-10
; PRIOR APPLICATION NUMBER: US 60/344,692
; PRIOR FILING DATE: 2001-10-19
; PRIOR APPLICATION NUMBER: US 60/387,292
; PRIOR FILING DATE: 2002-06-07
; PRIOR APPLICATION NUMBER: US 60/391,777
; PRIOR FILING DATE: 2002-06-25
; PRIOR APPLICATION NUMBER: US 60/396,594
; PRIOR FILING DATE: 2002-07-17
; PRIOR APPLICATION NUMBER: US 60/404,249
; PRIOR FILING DATE: 2002-08-16
; PRIOR APPLICATION NUMBER: US 60/407,527
; NUMBER OF SEQ ID NOS: 75
; SOFTWARE: PatentIn version 3.2
; SEQ ID NO 73
; LENGTH: 165
; TYPE: PRT
; ORGANISM: Homo sapiens
US-10-411-026-73

Query Match      100.0%; Score 846; DB 15; Length 165;
Best Local Similarity 100.0%; Pred. No. 1.4e-85;
Matches 165; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

QY 1 APPRLICDSRVLYRLLEAKEAENITTCGAHCSSLNENITVPDTKYNFYAWKMEVGGQA 60
DB 1 APPRLICDSRVLYRLLEAKEAENITTCGAHCSSLNENITVPDTKYNFYAWKMEVGGQA 60
QY 61 VEVWQGLALLSEAVLRGQALLVNSSQPWEPLQLHVDKAVSGRLSLTTLRALGAQKEAIS 120
DB 61 VEVWQGLALLSEAVLRGQALLVNSSQPWEPLQLHVDKAVSGRLSLTTLRALGAQKEAIS 120
QY 121 PPDAASAAPLRTITADTFKFLFRVYSNFLRGKLYTGACRTGD 165
DB 121 PPDAASAAPLRTITADTFKFLFRVYSNFLRGKLYTGACRTGD 165
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QY 1 APPRLICDSRVLYLLEAKEAENITTCGAHCSLNENITVPDTKVFYAWKMEVGGQA 60
Db 1 APPRLICDSRVLYLLEAKEAENITTCGAHCSLNENITVPDTKVFYAWKMEVGGQA 60
QY 61 VEVWQGLALLSEAVLRGQALLVNSSQPWEPLQHLVDKAVSGLRSLTTLRALGAQKEAIS 120
Db 61 VEVWQGLALLSEAVLRGQALLVNSSQPWEPLQHLVDKAVSGLRSLTTLRALGAQKEAIS 120
QY 121 PPDAASAAPLRTITADTFKLPVYSNLFRLGKLYTGACRTGD 165
Db 121 PPDAASAAPLRTITADTFKLPVYSNLFRLGKLYTGACRTGD 165

RESULT 11
US-10-410-930-73
; Sequence 73, Application US/10410930
; Publication No. US20040115168A1
; GENERAL INFORMATION:
; APPLICANT: Neose Technologies, Inc.
; APPLICANT: DePrees, Shawn
; APPLICANT: Zopf, David
; APPLICANT: Bayer, Robert
; APPLICANT: Hakes, David
; APPLICANT: Chen, Xi
; APPLICANT: Bowe, Caryn
; TITLE OF INVENTION: INTERFERON BETA: REMODELING AND GLYCOCONJUGATION OF INTERFERON
; FILE REFERENCE: 040853-01-5056
; CURRENT APPLICATION NUMBER: US/10/410,930
; CURRENT FILING DATE: 2003-04-09
; PRIOR APPLICATION NUMBER: US 60/328,523
; PRIOR FILING DATE: 2001-10-10
; PRIOR APPLICATION NUMBER: US 60/344,692
; PRIOR FILING DATE: 2001-10-19
; PRIOR APPLICATION NUMBER: US 60/387,292
; PRIOR FILING DATE: 2002-06-07
; PRIOR APPLICATION NUMBER: US 60/391,777
; PRIOR FILING DATE: 2002-06-25
; PRIOR APPLICATION NUMBER: US 60/396,594
; PRIOR FILING DATE: 2002-07-17
; PRIOR APPLICATION NUMBER: US 60/404,249
; PRIOR FILING DATE: 2002-08-16
; PRIOR APPLICATION NUMBER: US 60/407,527
; PRIOR FILING DATE: 2002-08-28
; NUMBER OF SEQ ID NOS: 75
; SOFTWARE: PatentIn version 3.2
; SEQ ID NO 73
; LENGTH: 165
; TYPE: PRT
; ORGANISM: Homo sapiens
US-10-410-930-73

Query Match 100.0%; Score 846; DB 16; Length 165;
Best Local Similarity 100.0%; Pred. No. 1.4e-85;
Matches 165; Conservative 0; Mismatches 0; Indels 0; Gaps 0;
QY 1 APPRLICDSRVLYLLEAKEAENITTCGAHCSLNENITVPDTKVFYAWKMEVGGQA 60
Db 1 APPRLICDSRVLYLLEAKEAENITTCGAHCSLNENITVPDTKVFYAWKMEVGGQA 60
QY 61 VEVWQGLALLSEAVLRGQALLVNSSQPWEPLQHLVDKAVSGLRSLTTLRALGAQKEAIS 120
Db 61 VEVWQGLALLSEAVLRGQALLVNSSQPWEPLQHLVDKAVSGLRSLTTLRALGAQKEAIS 120
QY 121 PPDAASAAPLRTITADTFKLPVYSNLFRLGKLYTGACRTGD 165
Db 121 PPDAASAAPLRTITADTFKLPVYSNLFRLGKLYTGACRTGD 165

RESULT 12
US-10-410-997-73
; Sequence 73, Application US/10410997
; Publication No. US20040126838A1

GENERAL INFORMATION:
; APPLICANT: Neose Technologies, Inc.
; APPLICANT: DePrees, Shawn
; APPLICANT: Zopf, David
; APPLICANT: Bayer, Robert
; APPLICANT: Hakes, David
; APPLICANT: Chen, Xi
; APPLICANT: Bowe, Caryn
; TITLE OF INVENTION: FOLLICLE STIMULATING HORMONE: REMODELING AND GLYCOCONJUGATION OF
; FILE REFERENCE: 040853-01-5059
; CURRENT APPLICATION NUMBER: US/10/410,997
; CURRENT FILING DATE: 2003-04-09
; PRIOR APPLICATION NUMBER: US 60/328,523
; PRIOR FILING DATE: 2001-10-10
; PRIOR APPLICATION NUMBER: US 60/344,692
; PRIOR FILING DATE: 2001-10-19
; PRIOR APPLICATION NUMBER: US 60/387,292
; PRIOR FILING DATE: 2002-06-07
; PRIOR APPLICATION NUMBER: US 60/391,777
; PRIOR FILING DATE: 2002-06-25
; PRIOR APPLICATION NUMBER: US 60/396,594
; PRIOR FILING DATE: 2002-07-17
; PRIOR APPLICATION NUMBER: US 60/404,249
; PRIOR FILING DATE: 2002-08-16
; PRIOR APPLICATION NUMBER: US 60/407,527
; PRIOR FILING DATE: 2002-08-28
; NUMBER OF SEQ ID NOS: 75
; SOFTWARE: PatentIn version 3.2
; SEQ ID NO 73
; LENGTH: 165
; TYPE: PRT
; ORGANISM: Homo sapiens
US-10-410-997-73

Query Match 100.0%; Score 846; DB 16; Length 165;
Best Local Similarity 100.0%; Pred. No. 1.4e-85;
Matches 165; Conservative 0; Mismatches 0; Indels 0; Gaps 0;
QY 1 APPRLICDSRVLYLLEAKEAENITTCGAHCSLNENITVPDTKVFYAWKMEVGGQA 60
Db 1 APPRLICDSRVLYLLEAKEAENITTCGAHCSLNENITVPDTKVFYAWKMEVGGQA 60
QY 61 VEVWQGLALLSEAVLRGQALLVNSSQPWEPLQHLVDKAVSGLRSLTTLRALGAQKEAIS 120
Db 61 VEVWQGLALLSEAVLRGQALLVNSSQPWEPLQHLVDKAVSGLRSLTTLRALGAQKEAIS 120
QY 121 PPDAASAAPLRTITADTFKLPVYSNLFRLGKLYTGACRTGD 165
Db 121 PPDAASAAPLRTITADTFKLPVYSNLFRLGKLYTGACRTGD 165

RESULT 13
US-10-411-012-73
; Sequence 73, Application US/10411012
; Publication No. US20040132840A1
; GENERAL INFORMATION:
; APPLICANT: Neose Technologies, Inc.
; APPLICANT: DePrees, Shawn
; APPLICANT: Zopf, David
; APPLICANT: Bayer, Robert
; APPLICANT: Hakes, David
; APPLICANT: Chen, Xi
; APPLICANT: Bowe, Caryn
; TITLE OF INVENTION: GLYCOEGLYATION METHODS AND PROTEINS/PEPTIDES PRODUCED BY THE
; FILE REFERENCE: 040853-01-5051
; CURRENT APPLICATION NUMBER: US/10/411,012
; CURRENT FILING DATE: 2003-04-09
; PRIOR APPLICATION NUMBER: US 60/328,523
; PRIOR FILING DATE: 2001-10-10
; PRIOR APPLICATION NUMBER: US 60/344,692
; PRIOR FILING DATE: 2001-10-19

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; PRIOR APPLICATION NUMBER: US 60/328,523
; PRIOR FILING DATE: 2001-10-10
; PRIOR APPLICATION NUMBER: US 60/344,692
; PRIOR FILING DATE: 2001-10-19
; PRIOR APPLICATION NUMBER: US 60/387,292
; PRIOR FILING DATE: 2002-06-07
; PRIOR APPLICATION NUMBER: US 60/391,777
; PRIOR FILING DATE: 2002-06-25
; PRIOR APPLICATION NUMBER: US 60/396,594
; PRIOR FILING DATE: 2002-07-17
; PRIOR APPLICATION NUMBER: US 60/404,249
; PRIOR FILING DATE: 2002-08-16
; PRIOR APPLICATION NUMBER: US 60/407,527
; PRIOR FILING DATE: 2002-08-28
; NUMBER OF SEQ ID NOS: 75
; SOFTWARE: PatentIn version 3.2
; SEQ ID NO 73
; TYPE: PRT
; ORGANISM: Homo sapiens
US-10-410-980-73

Query Match      100.0%; Score 846; DB 17; Length 165;
Best Local Similarity 100.0%; Pred. No. 1.4e-85;
Matches 165; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

QY 1 APPRLICDSRVLEKAEENITTCAGHCSLNENITVPDTKVFYAWKMEVGGQA 60
DB 1 APPRLICDSRVLEKAEENITTCAGHCSLNENITVPDTKVFYAWKMEVGGQA 60
QY 61 VEVWQGLALLSEAVLRGQALLVNSQPWEPLQLHVDKAVSGLRSLTLLRALGAQKEAIS 120
DB 61 VEVWQGLALLSEAVLRGQALLVNSQPWEPLQLHVDKAVSGLRSLTLLRALGAQKEAIS 120
QY 121 PPDAASAAPLRTITADTFRKLFPRVYSNFRGLKLYTGACRTGD 165
DB 121 PPDAASAAPLRTITADTFRKLFPRVYSNFRGLKLYTGACRTGD 165

RESULT 17
US-10-410-897-73
; Sequence 73, Application US/10410897
; Publication No. US20050100982A1
; GENERAL INFORMATION:
; APPLICANT: Neose Technologies, Inc.
; APPLICANT: DeFrees, Shawn
; APPLICANT: Zopf, David
; APPLICANT: Bayer, Robert
; APPLICANT: Hakes, David
; APPLICANT: Chen, Xi
; APPLICANT: Rowe, Caryn
; TITLE OF INVENTION: FACTOR IX; REMODELING AND GLYCOCONJUGATION OF FACTOR IX
; FILE REFERENCE: 040853-01-5058
; CURRENT APPLICATION NUMBER: US/10/410,897
; CURRENT FILING DATE: 2003-04-09
; PRIOR APPLICATION NUMBER: US 60/328,523
; PRIOR FILING DATE: 2001-10-10
; PRIOR APPLICATION NUMBER: US 60/344,692
; PRIOR FILING DATE: 2001-10-19
; PRIOR APPLICATION NUMBER: US 60/387,292
; PRIOR FILING DATE: 2002-06-07
; PRIOR APPLICATION NUMBER: US 60/391,777
; PRIOR FILING DATE: 2002-06-25
; PRIOR APPLICATION NUMBER: US 60/396,594
; PRIOR FILING DATE: 2002-07-17
; PRIOR APPLICATION NUMBER: US 60/404,249
; PRIOR FILING DATE: 2002-08-16
; PRIOR APPLICATION NUMBER: US 60/407,527
; PRIOR FILING DATE: 2002-08-28
; NUMBER OF SEQ ID NOS: 75
; SOFTWARE: PatentIn version 3.2
; SEQ ID NO 73
; LENGTH: 165
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; TYPE: PRT
; ORGANISM: Homo sapiens
US-10-410-897-73

Query Match      100.0%; Score 846; DB 17; Length 165;
Best Local Similarity 100.0%; Pred. No. 1.4e-85;
Matches 165; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

QY 1 APPRLICDSRVLEKAEENITTCAGHCSLNENITVPDTKVFYAWKMEVGGQA 60
DB 1 APPRLICDSRVLEKAEENITTCAGHCSLNENITVPDTKVFYAWKMEVGGQA 60
QY 61 VEVWQGLALLSEAVLRGQALLVNSQPWEPLQLHVDKAVSGLRSLTLLRALGAQKEAIS 120
DB 61 VEVWQGLALLSEAVLRGQALLVNSQPWEPLQLHVDKAVSGLRSLTLLRALGAQKEAIS 120
QY 121 PPDAASAAPLRTITADTFRKLFPRVYSNFRGLKLYTGACRTGD 165
DB 121 PPDAASAAPLRTITADTFRKLFPRVYSNFRGLKLYTGACRTGD 165

RESULT 18
US-10-780-297-1
; Sequence 1, Application US/10780297
; Publication No. US20040147431A1
; GENERAL INFORMATION:
; APPLICANT: Papadimitriou, Apollon
; TITLE OF INVENTION: Erythropoietin Composition
; FILE REFERENCE: 20619 US
; CURRENT APPLICATION NUMBER: US/10/780,297
; CURRENT FILING DATE: 2004-02-17
; PRIOR APPLICATION NUMBER: US/09/853,731
; PRIOR FILING DATE: 2001-05-11
; PRIOR APPLICATION NUMBER: EP/00110355.5
; PRIOR FILING DATE: 2000-05-15
; NUMBER OF SEQ ID NOS: 2
; SOFTWARE: PatentIn version 3.0
; SEQ ID NO 1
; LENGTH: 165
; TYPE: PRT
; ORGANISM: Homo sapiens
US-10-780-297-1

Query Match      100.0%; Score 846; DB 18; Length 165;
Best Local Similarity 100.0%; Pred. No. 1.4e-85;
Matches 165; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

QY 1 APPRLICDSRVLEKAEENITTCAGHCSLNENITVPDTKVFYAWKMEVGGQA 60
DB 1 APPRLICDSRVLEKAEENITTCAGHCSLNENITVPDTKVFYAWKMEVGGQA 60
QY 61 VEVWQGLALLSEAVLRGQALLVNSQPWEPLQLHVDKAVSGLRSLTLLRALGAQKEAIS 120
DB 61 VEVWQGLALLSEAVLRGQALLVNSQPWEPLQLHVDKAVSGLRSLTLLRALGAQKEAIS 120
QY 121 PPDAASAAPLRTITADTFRKLFPRVYSNFRGLKLYTGACRTGD 165
DB 121 PPDAASAAPLRTITADTFRKLFPRVYSNFRGLKLYTGACRTGD 165

RESULT 19
US-09-853-731-2
; Sequence 2, Application US/09853731
; Patent No. US20020037841A1
; GENERAL INFORMATION:
; APPLICANT: Papadimitriou, Apollon
; TITLE OF INVENTION: Erythropoietin Composition
; FILE REFERENCE: 20619 US
; CURRENT APPLICATION NUMBER: US/09/853,731
; CURRENT FILING DATE: 2001-05-11
; PRIOR APPLICATION NUMBER: EP/00110355.5
; PRIOR FILING DATE: 2000-05-15
; NUMBER OF SEQ ID NOS: 2
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RESULT 23
US-10-400-377-2
; Sequence 2, Application US/10400377
; Publication No. US20030162949A1
; GENERAL INFORMATION:
; APPLICANT: Cox III, George N
; TITLE OF INVENTION: Derivatives of Growth Hormone and Related Proteins
; FILE REFERENCE: 4152-1-PUS
; CURRENT APPLICATION NUMBER: US/10/400,377
; PRIOR FILING DATE: 2003-03-26
; PRIOR APPLICATION NUMBER: US/09/462,941
; PRIOR FILING DATE: 2000-01-14
; PRIOR APPLICATION NUMBER: 60/052,516
; PRIOR FILING DATE: 1997-07-14
; NUMBER OF SEQ ID NOS: 41
; SOFTWARE: Patent In Ver. 2.0
; SEQ ID NO 2
; LENGTH: 166
; TYPE: PRT
; ORGANISM: Homo sapiens
US-10-400-377-2

Query Match      100.0%; Score 846; DB 14; Length 166;
Best Local Similarity 100.0%; Pred. No. 1.4e-85;
Matches 165; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

Qy 1 APPRLICDSRVLYRLLLEAKAENITTCGAHCNSLNENITVPTKVFYAKRMEVGQQA 60
Db 1 APPRLICDSRVLYRLLLEAKAENITTCGAHCNSLNENITVPTKVFYAKRMEVGQQA 60

Qy 61 VEVWQGLALLSEAVLRGQALLVNSSQPWEPLQLHVDKAVSGLSRLTTLRALGAQKEAIS 120
Db 61 VEVWQGLALLSEAVLRGQALLVNSSQPWEPLQLHVDKAVSGLSRLTTLRALGAQKEAIS 120

Qy 121 PPDAASAAPLRTITADTFKFLFRVYSNPLRGKLYTGEACRTGD 165
Db 121 PPDAASAAPLRTITADTFKFLFRVYSNPLRGKLYTGEACRTGD 165

RESULT 24
US-10-400-708-2
; Sequence 2, Application US/10400708
; Publication No. US20030166865A1
; GENERAL INFORMATION:
; APPLICANT: Cox III, George N
; TITLE OF INVENTION: Derivatives of Growth Hormone and Related Proteins
; FILE REFERENCE: 4152-1-PUS
; CURRENT APPLICATION NUMBER: US/10/400,708
; CURRENT FILING DATE: 2003-03-26
; PRIOR APPLICATION NUMBER: US/09/462,941
; PRIOR FILING DATE: 2000-01-14
; PRIOR APPLICATION NUMBER: 60/052,516
; PRIOR FILING DATE: 1997-07-14
; NUMBER OF SEQ ID NOS: 41
; SOFTWARE: Patent In Ver. 2.0
; SEQ ID NO 2
; LENGTH: 166
; TYPE: PRT
; ORGANISM: Homo sapiens
US-10-400-708-2

Query Match      100.0%; Score 846; DB 14; Length 166;
Best Local Similarity 100.0%; Pred. No. 1.4e-85;
Matches 165; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

Qy 1 APPRLICDSRVLYRLLLEAKAENITTCGAHCNSLNENITVPTKVFYAKRMEVGQQA 60
Db 1 APPRLICDSRVLYRLLLEAKAENITTCGAHCNSLNENITVPTKVFYAKRMEVGQQA 60

Qy 61 VEVWQGLALLSEAVLRGQALLVNSSQPWEPLQLHVDKAVSGLSRLTTLRALGAQKEAIS 120
Db 61 VEVWQGLALLSEAVLRGQALLVNSSQPWEPLQLHVDKAVSGLSRLTTLRALGAQKEAIS 120

Qy 121 PPDAASAAPLRTITADTFKFLFRVYSNPLRGKLYTGEACRTGD 165
Db 121 PPDAASAAPLRTITADTFKFLFRVYSNPLRGKLYTGEACRTGD 165

RESULT 25
US-10-298-148-2
; Sequence 2, Application US/10298148
; Publication No. US20030171284A1
; GENERAL INFORMATION:
; APPLICANT: Cox III, George N
; TITLE OF INVENTION: Derivatives of Growth Hormone and Related Proteins
; FILE REFERENCE: 4152-1-PUS
; CURRENT APPLICATION NUMBER: US/10/298,148
; CURRENT FILING DATE: 2002-11-15
; PRIOR APPLICATION NUMBER: US/09/462,941
; PRIOR FILING DATE: 2000-01-14
; PRIOR APPLICATION NUMBER: 60/052,516
; PRIOR FILING DATE: 1997-07-14
; NUMBER OF SEQ ID NOS: 41
; SOFTWARE: Patent In Ver. 2.0
; SEQ ID NO 2
; LENGTH: 166
; TYPE: PRT
; ORGANISM: Homo sapiens
US-10-298-148-2

Query Match      100.0%; Score 846; DB 14; Length 166;
Best Local Similarity 100.0%; Pred. No. 1.4e-85;
Matches 165; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

Qy 1 APPRLICDSRVLYRLLLEAKAENITTCGAHCNSLNENITVPTKVFYAKRMEVGQQA 60
Db 1 APPRLICDSRVLYRLLLEAKAENITTCGAHCNSLNENITVPTKVFYAKRMEVGQQA 60

Qy 61 VEVWQGLALLSEAVLRGQALLVNSSQPWEPLQLHVDKAVSGLSRLTTLRALGAQKEAIS 120
Db 61 VEVWQGLALLSEAVLRGQALLVNSSQPWEPLQLHVDKAVSGLSRLTTLRALGAQKEAIS 120

Qy 121 PPDAASAAPLRTITADTFKFLFRVYSNPLRGKLYTGEACRTGD 165
Db 121 PPDAASAAPLRTITADTFKFLFRVYSNPLRGKLYTGEACRTGD 165

RESULT 26
US-10-360-101-227
; Sequence 227, Application US/10360101
; Publication No. US20040009550A1
; GENERAL INFORMATION:
; APPLICANT: Moll, Gert N.
; APPLICANT: Leenhouts, Cornelis J.
; TITLE OF INVENTION: Export and modification of (poly)peptide in the lantibiotic way
; FILE REFERENCE: 2183-5673
; CURRENT APPLICATION NUMBER: US/10/360,101
; CURRENT FILING DATE: 2003-02-07
; PRIOR APPLICATION NUMBER: EP 02077060.8
; PRIOR FILING DATE: 2002-05-24
; NUMBER OF SEQ ID NOS: 309
; SOFTWARE: Patent In version 3.1
; SEQ ID NO 227
; LENGTH: 166
; TYPE: PRT
; ORGANISM: Artificial Sequence
; FEATURE:
; OTHER INFORMATION: sequence of erythropoietin
US-10-360-101-227

Query Match      100.0%; Score 846; DB 15; Length 166;
Best Local Similarity 100.0%; Pred. No. 1.4e-85;

```

Dd 121 PPDAASAAPLRTITADTFKRLFRVYSNFLRGKLKYTGACRTGD 165

RESULT 30
US-10-774-149-2
; Sequence 2, Application US/10774149
; Publication No. US20040175800A1
; GENERAL INFORMATION:
; APPLICANT: Cox III, George N
; TITLE OF INVENTION: Derivatives of Growth Hormone and Related Proteins
; FILE REFERENCE: 4152-1-PUS
; CURRENT APPLICATION NUMBER: US/10/774,149
; CURRENT FILING DATE: 2004-02-05
; PRIOR APPLICATION NUMBER: US/10/400,377
; PRIOR FILING DATE: 2003-03-26
; PRIOR APPLICATION NUMBER: US/09/462,941
; PRIOR FILING DATE: 2000-01-14
; PRIOR APPLICATION NUMBER: 60/052,516
; PRIOR FILING DATE: 1997-07-14
; NUMBER OF SEQ ID NOS: 41
; SOFTWARE: PatentIn Ver. 2.0
; SEQ ID NO 2
; LENGTH: 166
; TYPE: PRT
; ORGANISM: Homo sapiens
US-10-774-149-2

Query Match 100.0%; Score 846; DB 16; Length 166;
Best Local Similarity 100.0%; Pred. No. 1.4e-85;
Matches 165; Conservative 0; Mismatches 0; Indels 0; Gaps 0

Qy 1 APRPLCDSRVLRYLLBAKEAENITTCGAHCSLNENITVPDTKNFYAWKRMEVGQA 60
| | | | |
Db 1 APRPLCDSRVLRYLLBAKEAENITTCGAHCSLNENITVPDTKNFYAWKRMEVGQA 60
| | | | |

Qy 61 VEVWQGLALLSEAVLRGQALLVNSSQPWEPLQLHVVDKAVSLRSLTTLRALGAQKEATS 120
| | | | |
Db 61 VEVWQGLALLSEAVLRGQALLVNSSQPWEPLQLHVVDKAVSLRSLTTLRALGAQKEATS 120
| | | | |

Qy 121 PPDAASAAPLRTITADTFKRLFRVYSNFLRGKLKYTGACRTGD 165
| | | | |
Db 121 PPDAASAAPLRTITADTFKRLFRVYSNFLRGKLKYTGACRTGD 165
| | | | |

RESULT 31
US-10-468-496-133
; Sequence 133, Application US/10468496
; Publication No. US20040180386A1
; GENERAL INFORMATION:
; APPLICANT: Carr, Francis J.
; APPLICANT: Carter, Graham
; APPLICANT: Jones, Tim
; APPLICANT: Williams, Stephen
; APPLICANT: Hamilton, Anita
; TITLE OF INVENTION: METHOD FOR IDENTIFICATION OF T-CELL
; TITLE OF INVENTION: EPITOPE AND USE FOR PREPARING MOLECULES WITH REDUCED
; TITLE OF INVENTION: IMMUNOGENICITY
; FILE REFERENCE: MER-117
; CURRENT APPLICATION NUMBER: US/10/468,496
; CURRENT FILING DATE: 2003-09-25
; PRIOR APPLICATION NUMBER: 01103954.2
; PRIOR FILING DATE: 2001-02-19
; PRIOR APPLICATION NUMBER: 01105777.5
; PRIOR FILING DATE: 2001-03-08
; PRIOR APPLICATION NUMBER: 01106538.0
; PRIOR FILING DATE: 2001-03-15
; PRIOR APPLICATION NUMBER: 01106536.4
; PRIOR FILING DATE: 2001-03-15
; PRIOR APPLICATION NUMBER: 01107012.5
; PRIOR FILING DATE: 2001-03-20
; PRIOR APPLICATION NUMBER: 01106899.6
; PRIOR FILING DATE: 2001-03-20


```
; CURRENT FILING DATE: 2004-06-10
; PRIOR APPLICATION NUMBER: US/10/400,377
; PRIOR FILING DATE: 2003-03-26
; PRIOR APPLICATION NUMBER: US/09/462,941
; PRIOR FILING DATE: 2000-01-14
; PRIOR APPLICATION NUMBER: 60/052,516
; PRIOR FILING DATE: 1997-07-14
; NUMBER OF SEQ ID NOS: 41
; SOFTWARE: Patent in Ver. 2.0
; SEQ ID NO 2
; LENGTH: 166
; TYPE: PRT
; ORGANISM: Homo sapiens
US-10-866-580-2

Query Match      100.0%; Score 846; DB 17; Length 166;
Best Local Similarity 100.0%; Pred. No. 1.4e-85;
Matches 165; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

QY 1 APPRLICDSRVLEKAEAEENITTCAGHCSLNENITVPDVKVNFYAKRMEVGQQA 60
DB 1 APPRLICDSRVLEKAEAEENITTCAGHCSLNENITVPDVKVNFYAKRMEVGQQA 60

QY 61 VEVWQGLALLSEAVLRGQALLVNSQPWEPLQLHVDKAVSGLSLTTLLRALGAQKEAIS 120
DB 61 VEVWQGLALLSEAVLRGQALLVNSQPWEPLQLHVDKAVSGLSLTTLLRALGAQKEAIS 120

QY 121 PPDAASAAPLRITADTFKFLFRVYSNFLRGLKLYTGACRTGD 165
DB 121 PPDAASAAPLRITADTFKFLFRVYSNFLRGLKLYTGACRTGD 165

RESULT 37
US-10-773-530-2
; Sequence 2, Application US/10773530
; Publication No. US20050107591A1
; GENERAL INFORMATION:
; APPLICANT: Cox III, George N
; APPLICANT: Bolder Biotechnology, Inc.
; TITLE OF INVENTION: Derivatives of Growth Hormone and Related Proteins
; FILE REFERENCE: 4152-1-PUS
; CURRENT APPLICATION NUMBER: US/10/773,530
; PRIOR FILING DATE: 2004-02-05
; PRIOR APPLICATION NUMBER: US/10/400,377
; PRIOR FILING DATE: 2003-03-26
; PRIOR APPLICATION NUMBER: US/09/462,941
; PRIOR FILING DATE: 2000-01-14
; PRIOR APPLICATION NUMBER: 60/052,516
; PRIOR FILING DATE: 1997-07-14
; NUMBER OF SEQ ID NOS: 41
; SOFTWARE: Patent in Ver. 2.0
; SEQ ID NO 2
; LENGTH: 166
; TYPE: PRT
; ORGANISM: Homo sapiens
US-10-773-530-2

Query Match      100.0%; Score 846; DB 17; Length 166;
Best Local Similarity 100.0%; Pred. No. 1.4e-85;
Matches 165; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

QY 1 APPRLICDSRVLEKAEAEENITTCAGHCSLNENITVPDVKVNFYAKRMEVGQQA 60
DB 1 APPRLICDSRVLEKAEAEENITTCAGHCSLNENITVPDVKVNFYAKRMEVGQQA 60

QY 61 VEVWQGLALLSEAVLRGQALLVNSQPWEPLQLHVDKAVSGLSLTTLLRALGAQKEAIS 120
DB 61 VEVWQGLALLSEAVLRGQALLVNSQPWEPLQLHVDKAVSGLSLTTLLRALGAQKEAIS 120

QY 121 PPDAASAAPLRITADTFKFLFRVYSNFLRGLKLYTGACRTGD 165
DB 121 PPDAASAAPLRITADTFKFLFRVYSNFLRGLKLYTGACRTGD 165
```

RESULT 38

```
US-10-780-297-2
; Sequence 2, Application US/10780297
; Publication No. US20040147431A1
; GENERAL INFORMATION:
; APPLICANT: Papadimitriou, Apollon
; TITLE OF INVENTION: Erythropoietin Composition
; FILE REFERENCE: 20619 US
; CURRENT APPLICATION NUMBER: US/10/780,297
; CURRENT FILING DATE: 2004-02-17
; PRIOR APPLICATION NUMBER: US/09/853,731
; PRIOR FILING DATE: 2001-05-11
; PRIOR APPLICATION NUMBER: EP/00110355.5
; PRIOR FILING DATE: 2000-05-15
; NUMBER OF SEQ ID NOS: 2
; SOFTWARE: Patent in version 3.0
; SEQ ID NO 2
; LENGTH: 166
; TYPE: PRT
; ORGANISM: Homo sapiens
US-10-780-297-2
```

```
Query Match      100.0%; Score 846; DB 18; Length 166;
Best Local Similarity 100.0%; Pred. No. 1.4e-85;
Matches 165; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

QY 1 APPRLICDSRVLEKAEAEENITTCAGHCSLNENITVPDVKVNFYAKRMEVGQQA 60
DB 1 APPRLICDSRVLEKAEAEENITTCAGHCSLNENITVPDVKVNFYAKRMEVGQQA 60

QY 61 VEVWQGLALLSEAVLRGQALLVNSQPWEPLQLHVDKAVSGLSLTTLLRALGAQKEAIS 120
DB 61 VEVWQGLALLSEAVLRGQALLVNSQPWEPLQLHVDKAVSGLSLTTLLRALGAQKEAIS 120

QY 121 PPDAASAAPLRITADTFKFLFRVYSNFLRGLKLYTGACRTGD 165
DB 121 PPDAASAAPLRITADTFKFLFRVYSNFLRGLKLYTGACRTGD 165
```

RESULT 39

```
US-10-014-363-4
; Sequence 4, Application US/10014363
; Publication No. US20020115833A1
; GENERAL INFORMATION:
; APPLICANT: Burg, Josef
; APPLICANT: Engel, Alfred
; APPLICANT: Franze, Reinhard
; APPLICANT: Hilger, Bernd
; APPLICANT: Schurig, Hartmut Ernst
; APPLICANT: Tischer, Wilhelm
; APPLICANT: Wozny, Manfred
; TITLE OF INVENTION: Erythropoietin Conjugates
; FILE REFERENCE: Case 20805
; CURRENT APPLICATION NUMBER: US/10/014,363
; CURRENT FILING DATE: 2001-12-11
; NUMBER OF SEQ ID NOS: 5
; SOFTWARE: Patent in version 3.1
; SEQ ID NO 4
; LENGTH: 169
; TYPE: PRT
; ORGANISM: CHO/dhfr-
US-10-014-363-4
```

```
Query Match      100.0%; Score 846; DB 13; Length 169;
Best Local Similarity 100.0%; Pred. No. 1.4e-85;
Matches 165; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

QY 1 APPRLICDSRVLEKAEAEENITTCAGHCSLNENITVPDVKVNFYAKRMEVGQQA 60
DB 4 APPRLICDSRVLEKAEAEENITTCAGHCSLNENITVPDVKVNFYAKRMEVGQQA 63

QY 61 VEVWQGLALLSEAVLRGQALLVNSQPWEPLQLHVDKAVSGLSLTTLLRALGAQKEAIS 120
```

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; PRIOR FILING DATE: 2002-01-04
; PRIOR APPLICATION NUMBER: US 60/358,598
; PRIOR FILING DATE: 2002-02-21
; NUMBER OF SEQ ID NOS: 22
; SOFTWARE: PatentIn version 3.1
; SEQ ID NO 2
; LENGTH: 193
;

```

; ORGANISM: Homo sapiens
 US-10-113-824-2

	Query Match	100.0%	Score 846;	DB 14;	Length 193;
	Best Local Similarity	100.0%;	0;	Mismatches 0;	Indels 0;
	Matches 165;	Conservative	0;	Mismatches 0;	Indels 0;
Qy	1	APPLICDSRVLYRLLEAKEAENITTCGCAHCSLNENITVPDTKVFYAKRWMEVGGQA	60		
Db	28	APPLICDSRVLYRLLEAKEAENITTCGCAHCSLNENITVPDTKVFYAKRWMEVGGQA	87		
Qy	61	VEVWQGLALLSEAVLRGQALLVNSSQWPEIQLHVDKAVSGLSRLTILLRALGAKQKAIS	120		
Db	88	VEVWQGLALLSEAVLRGQALLVNSSQWPEIQLHVDKAVSGLSRLTILLRALGAKQKAIS	147		
Qy	121	PPDAASAPRLTTTADTFRKLFRVYSNPLRGKLLYTGEACRTGD	165		
Db	148	PPDAASAPRLTTTADTFRKLFRVYSNPLRGKLLYTGEACRTGD	192		

RESULT 44

US-10-612-665-10
; Sequence 10, Application US/10612665
; Publication No. US20040122216A1
; GENERAL INFORMATION:
; APPLICANT: Nielsen, J
; APPLICANT: Pedersen, J.
; APPLICANT: Gerwien, J.
; APPLICANT: Bay, K.
; APPLICANT: Pedersen, L.
; APPLICANT: Leist, M.
; APPLICANT: Geist, M.
; APPLICANT: Kallunki, P.
; APPLICANT: Christensen, S.
; APPLICANT: Sager, T.
; APPLICANT: Brines, M.
; APPLICANT: Cerami, A.
; APPLICANT: Cerami, C.
; TITLE OF INVENTION: RECOMBINANT TISSUE PROTECTIVE CYTOKINES AND ENCODING NUCLEIC
; TITLE OF INVENTION: ACIDS THEREOF FOR PROTECTION, RESTORATION, AND ENHANCEMENT OF
; FILE REFERENCE: 10165-022-999
; CURRENT APPLICATION NUMBER: US/10/612,665
; CURRENT FILING DATE: 2003-07-01
; PRIOR APPLICATION NUMBER: 60/392,455
; PRIOR FILING DATE: 2002-07-01
; PRIOR APPLICATION NUMBER: 60/393,423
; PRIOR FILING DATE: 2002-07-03
; NUMBER OF SEQ ID NOS: 212
; SOFTWARE: PatentIn version 3.2
; SEQ ID NO 10
; LENGTH: 193
; TYPE: PRT
; ORGANISM: Homo sapiens
US-10-612-665-10

	Query Match	Best Local Similarity	Score	DB 16;	Length	193;
	Matches 165;	Conservative 0;	Mismatches 0;	Indels 0;	Gaps 0	
QY	1	APPRLICDSRVLYRLLLEAKAEENITTCGAEHCISLNEENITVPDPTKNFVAKRMEVGOQA	60			
DB	28	APPRLICDSRVLYRLLLEAKAEENITTCGAEHCISLNEENITVPDPTKNFVAKRMEVGOQA	87			
QY	61	VEVWQGLALLSEAVLRGQALLVNSQSQPEQLQLHVDKAVSLGRSLTTLFALGAKOEKLS	120			

Db	88	VEVQGLALLSEAVLRQALLVNSSQWPEPIQLHVDKAVSGLSRITLLRALGQKEAIS	147
Qy	121	PPDAASAAPRTTTADTFRLFRVYSNPLRGKLLKLTGEACRTGD	165
Db	148	PPDAASAAPRTTTADTFRLFRVYSNPLRGKLLKLTGEACRTGD	192

RESULT 45

```

US-10-612-665-22
; Sequence 22, Application US/10612665
; Publication No. US20040122216A1
; GENERAL INFORMATION:
; APPLICANT: Nielsen, J.
; APPLICANT: Pedersen, J.
; APPLICANT: Gerwien, J.
; APPLICANT: Bay, K.
; APPLICANT: Pedersen, L.
; APPLICANT: Leist, M.
; APPLICANT: Geist, M.
; APPLICANT: Kallunki, P.
; APPLICANT: Christensen, S.
; APPLICANT: Sager, T.
; APPLICANT: Brines, M.
; APPLICANT: Cerami, A.
; APPLICANT: Cerami, C.
; TITLE OF INVENTION: RECOMBINANT TISSUE PROTECTIVE CYTOKINES AND ENCODING NUCLEIC
; TITLE OF INVENTION: ACIDS THEREOF FOR PROTECTION, AND ENHANCEMENT OF
; FILE REFERENCE: 10165-022-999
; CURRENT APPLICATION NUMBER: US/10/612,665
; CURRENT FILING DATE: 2003-07-01
; PRIOR APPLICATION NUMBER: 60/392,455
; PRIOR FILING DATE: 2002-07-01
; PRIOR APPLICATION NUMBER: 60/393,423
; PRIOR FILING DATE: 2002-07-03
; NUMBER OF SEQ ID NOS: 212
; SOFTWARE: PatentIn version 3.2
; SEQ ID NO 22
; LENGTH: 193
; TYPE: PRT
; ORGANISM: Artificial
; FEATURE:
; OTHER INFORMATION: Description of Artificial Sequence: mutein
US-10-612-665-22

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```

/ / TITLE OF INVENTION: RECOMBINANT TISSUE PROTECTIVE CYTOKINES AND ENCODING NUCLEIC
/ /
/ / TITLE OF INVENTION: ACIDS THEREOF FOR PROTECTION, RESTORATION, AND ENHANCEMENT OF
/ /
/ / TITLE OF INVENTION: RESPONSIVE CELLS, TISSUES AND ORGANS
/ /
/ / FILE REFERENCE: 10165-022-999
/ /
/ / CURRENT APPLICATION NUMBER: US/10/612,665
/ /
/ / CURRENT FILING DATE: 2003-07-01
/ /
/ / PRIOR APPLICATION NUMBER: 60/392,455
/ /
/ / PRIOR FILING DATE: 2002-07-01
/ /
/ / PRIOR APPLICATION NUMBER: 60/393,423
/ /
/ / PRIOR FILING DATE: 2002-07-03
/ /
/ / NUMBER OF SEQ ID NOS: 212
/ /
/ / SOFTWARE: PatentIn version 3.2
/ /
/ / SEQ ID NO 10
/ /
/ / LENGTH: 193
/ /
/ / TYPE: PRT
/ /
/ / ORGANISM: Homo sapiens
/ /
/ / US-10-612-665-10

```

	Query Match	100.0%;	Score 846;	DB 16;	Length 193;
	Best Local Similarity	100.0%;	Pred. No. 1.7e-85;		
	Matches 165;	Conservative 0;	Mismatches 0;	Indels 0;	Gaps 0
Qy	1	APPRLLCDSRVLYRLLKAEENITTCGAHCHSLNENITVPDTKNFYAKWMEYGOOA	60		
Db	28	APPRLLCDSRVLYRLLKAEENITTCGAHCHSLNENITVPDTKNFYAKWMEYGOOA	87		
Qy	61	VEVWQGLALLSEAVLRGQALIVNSSQPWEIQLLHVDKAVSLGRSLTTLFALGAKOEATLS	120		

RESULT 46
US-10-612-665-112
; Sequence 112, Application US/10612665
; Publication No. US20040122216A1
; GENERAL INFORMATION:
; APPLICANT: Nielsen, J
; APPLICANT: Pedersen, J.
; APPLICANT: Gerwien, J.
; APPLICANT: Bay, K.
; APPLICANT: Pedersen, L.

; Publication No. US20040214236A1
 ; GENERAL INFORMATION:
 ; APPLICANT: Nielsen, M.
 ; APPLICANT: Gerwien, J.
 ; APPLICANT: Pedersen, L.
 ; APPLICANT: Leist, M.
 ; APPLICANT: Sager, T.
 ; APPLICANT: Brines, M.
 ; APPLICANT: Cerami, A.
 ; APPLICANT: Ghezzi, P.
 ; APPLICANT: Fiordaliso, F.
 ; APPLICANT: Fratelli, M.
 ; APPLICANT: Gido, G.
 ; TITLE OF INVENTION: TISSUE PROTECTIVE CYTOKINE RECEPTOR COMPLEX AND ASSAYS FOR IDENTIFICATION OF TISSUE PROTECTIVE COMPOUNDS
 ; FILE REFERENCE: 10165-027-999
 ; CURRENT APPLICATION NUMBER: US/10/676,694
 ; CURRENT FILING DATE: 2003-09-30
 ; PRIOR APPLICATION NUMBER: 60/465,891
 ; PRIOR FILING DATE: 2003-04-25
 ; NUMBER OF SEQ ID NOS: 212
 ; SOFTWARE: PatentIn version 3.2
 ; SEQ ID NO 112
 ; LENGTH: 193
 ; TYPE: PRT
 ; ORGANISM: Artificial
 ; FEATURE:
 ; OTHER INFORMATION: Description of Artificial Sequence: mutein
 US-10-676-694-112

 Query Match 100.0%; Score 846; DB 16; Length 193;
 Best Local Similarity 100.0%; Pred. No. 1.7e-85;
 Matches 165; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

 Qy 1 APPRLCDSRVLYRLLLEAKAEENITTCGAHCSLNENITVPDTKVNFYAKRMVEVGQQA 60
 Db 28 APPRLCDSRVLYRLLLEAKAEENITTCGAHCSLNENITVPDTKVNFYAKRMVEVGQQA 87

 Qy 61 VEVWQGLALLSEAVLRQALLVNSQPWEPLQLHVDKAVSGLRSILTLRLALGAKQKAIS 120
 Db 88 VEVWQGLALLSEAVLRQALLVNSQPWEPLQLHVDKAVSGLRSILTLRLALGAKQKAIS 147

 Qy 121 PPDAASAAPLRITATDFRKLFRVYSNFLRGKLYTGEACRTGD 165
 Db 148 PPDAASAAPLRITATDFRKLFRVYSNFLRGKLYTGEACRTGD 192

 RESULT 50
 US-10-759-031-10
 ; Sequence 10, Application US/10759031
 ; Publication No. US20050158822A1
 ; GENERAL INFORMATION:
 ; APPLICANT: Pecker, Iris
 ; TITLE OF INVENTION: HIGH LEVEL EXPRESSION OF RECOMBINANT HUMAN ERYTHROPOIETIN
 ; TITLE OF INVENTION: HAVING
 ; TITLE OF INVENTION: A MODIFIED 5'-UTR
 ; FILE REFERENCE: 27179
 ; CURRENT APPLICATION NUMBER: US/10/759,031
 ; CURRENT FILING DATE: 2004-01-20
 ; NUMBER OF SEQ ID NOS: 13
 ; SOFTWARE: PatentIn version 3.2
 ; SEQ ID NO 10
 ; LENGTH: 193
 ; TYPE: PRT
 ; ORGANISM: Homo sapiens
 US-10-759-031-10

 Query Match 100.0%; Score 846; DB 18; Length 193;
 Best Local Similarity 100.0%; Pred. No. 1.7e-85;
 Matches 165; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

 Qy 1 APPRLCDSRVLYRLLLEAKAEENITTCGAHCSLNENITVPDTKVNFYAKRMVEVGQQA 60

```
Query Match 100.0%; Score 846; DB 14; Length 220;
Best Local Similarity 100.0%; Pred. No. 2.1e-85;
Matches 165; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

QY 1 APPRLICDSRVLELYLEAKAEENITTCAGHCSLNENITVPDTKNFYAWKMEVGGQA 60
DB 28 APPRLICDSRVLELYLEAKAEENITTCAGHCSLNENITVPDTKNFYAWKMEVGGQA 87
QY 61 VEVWQGLALLSEAVLRGQALLVNSQPWEPLQHLHVDKAVSGLRSLTLLRALGAQKEAIS 120
DB 88 VEVWQGLALLSEAVLRGQALLVNSQPWEPLQHLHVDKAVSGLRSLTLLRALGAQKEAIS 147
QY 121 PPDASAAPLRITITADTFPKLFRVYSNFLRGKLYTGACRTGD 165
DB 148 PPDASAAPLRITITADTFPKLFRVYSNFLRGKLYTGACRTGD 192

RESULT 56
US-10-230-454-3
; Sequence 3, Application US/10230454
; Publication No. US20030124115A1
; GENERAL INFORMATION:
; APPLICANT: DONG-EOK, LEE
; APPLICANT: MYUNG-SUK, OH
; APPLICANT: BO-SUP, CHUNG
; APPLICANT: JI-SOOK, PARK
; APPLICANT: KI-WAN, KIM
; TITLE OF INVENTION: FUSION PROTEIN HAVING ENHANCED IN VIVO ACTIVITY OF
; FILE REFERENCE: ERYTHROPOIETIN
; CURRENT APPLICATION NUMBER: US/10/230,454
; PRIOR FILING DATE: 2002-08-29
; PRIOR APPLICATION NUMBER: 2001-74975
; NUMBER OF SEQ ID NOS: 18
; SOFTWARE: Patent In Ver. 2.1
; SEQ ID NO 3
; LENGTH: 370
; TYPE: PRT
; ORGANISM: Artificial Sequence
; OTHER INFORMATION: Description of Artificial Sequence: Fusion protein
; OTHER INFORMATION: (ELTP) of erythropoietin (EPO) and carboxy terminal
; OTHER INFORMATION: peptide (LTP) of human thrombopoietin
US-10-230-454-3

Query Match 100.0%; Score 846; DB 14; Length 370;
Best Local Similarity 100.0%; Pred. No. 4.2e-85;
Matches 165; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

QY 1 APPRLICDSRVLELYLEAKAEENITTCAGHCSLNENITVPDTKNFYAWKMEVGGQA 60
DB 28 APPRLICDSRVLELYLEAKAEENITTCAGHCSLNENITVPDTKNFYAWKMEVGGQA 87
QY 61 VEVWQGLALLSEAVLRGQALLVNSQPWEPLQHLHVDKAVSGLRSLTLLRALGAQKEAIS 120
DB 88 VEVWQGLALLSEAVLRGQALLVNSQPWEPLQHLHVDKAVSGLRSLTLLRALGAQKEAIS 147
QY 121 PPDASAAPLRITITADTFPKLFRVYSNFLRGKLYTGACRTGD 165
DB 148 PPDASAAPLRITITADTFPKLFRVYSNFLRGKLYTGACRTGD 192

RESULT 57
US-10-435-608-10
; Sequence 10, Application US/10435608
; Publication No. US20030235536A1
; GENERAL INFORMATION:
; APPLICANT: Blumberg, Richard S.
; APPLICANT: Lencer, Wayne I.
; APPLICANT: Simister, Neil E.
; APPLICANT: Bitonti, Alan J.
; TITLE OF INVENTION: CENTRAL AIRWAY ADMINISTRATION FOR SYSTEMIC DELIVERY OF THERAPEUTIC
```

```
; FILE REFERENCE: S01383.70010.US
; CURRENT APPLICATION NUMBER: US/10/435,608
; CURRENT FILING DATE: 2003-05-09
; PRIOR APPLICATION NUMBER: PCT/US02/21335
; PRIOR FILING DATE: 2002-07-03
; NUMBER OF SEQ ID NOS: 27
; SOFTWARE: Patent in version 3.1
; SEQ ID NO 10
; LENGTH: 428
; TYPE: PRT
; ORGANISM: Homo sapiens
US-10-435-608-10

Query Match 100.0%; Score 846; DB 15; Length 428;
Best Local Similarity 100.0%; Pred. No. 5.2e-85;
Matches 165; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

QY 1 APPRLICDSRVLELYLEAKAEENITTCAGHCSLNENITVPDTKNFYAWKMEVGGQA 60
DB 28 APPRLICDSRVLELYLEAKAEENITTCAGHCSLNENITVPDTKNFYAWKMEVGGQA 87
QY 61 VEVWQGLALLSEAVLRGQALLVNSQPWEPLQHLHVDKAVSGLRSLTLLRALGAQKEAIS 120
DB 88 VEVWQGLALLSEAVLRGQALLVNSQPWEPLQHLHVDKAVSGLRSLTLLRALGAQKEAIS 147
QY 121 PPDASAAPLRITITADTFPKLFRVYSNFLRGKLYTGACRTGD 165
DB 148 PPDASAAPLRITITADTFPKLFRVYSNFLRGKLYTGACRTGD 192

RESULT 58
US-10-622-108-10
; Sequence 10, Application US/10622108
; Publication No. US20040063912A1
; GENERAL INFORMATION:
; APPLICANT: Blumberg, Richard S.
; APPLICANT: Lencer, Wayne I.
; APPLICANT: Simister, Neil E.
; APPLICANT: Bitonti, Alan J.
; TITLE OF INVENTION: CENTRAL AIRWAY ADMINISTRATION FOR SYSTEMIC DELIVERY OF THERAPEUTIC
; FILE REFERENCE: S01383.70011.US
; CURRENT APPLICATION NUMBER: US/10/622,108
; CURRENT FILING DATE: 2003-07-17
; PRIOR APPLICATION NUMBER: US 10/435,608
; PRIOR FILING DATE: 2003-05-09
; PRIOR APPLICATION NUMBER: PCT/US02/21355
; PRIOR FILING DATE: 2002-07-03
; PRIOR APPLICATION NUMBER: US 60/364,482
; PRIOR FILING DATE: 2002-03-15
; NUMBER OF SEQ ID NOS: 40
; SOFTWARE: Patent in version 3.1
; SEQ ID NO 10
; LENGTH: 428
; TYPE: PRT
; ORGANISM: Homo sapiens
US-10-622-108-10

Query Match 100.0%; Score 846; DB 15; Length 428;
Best Local Similarity 100.0%; Pred. No. 5.2e-85;
Matches 165; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

QY 1 APPRLICDSRVLELYLEAKAEENITTCAGHCSLNENITVPDTKNFYAWKMEVGGQA 60
DB 28 APPRLICDSRVLELYLEAKAEENITTCAGHCSLNENITVPDTKNFYAWKMEVGGQA 87
QY 61 VEVWQGLALLSEAVLRGQALLVNSQPWEPLQHLHVDKAVSGLRSLTLLRALGAQKEAIS 120
DB 88 VEVWQGLALLSEAVLRGQALLVNSQPWEPLQHLHVDKAVSGLRSLTLLRALGAQKEAIS 147
QY 121 PPDASAAPLRITITADTFPKLFRVYSNFLRGKLYTGACRTGD 165
DB 148 PPDASAAPLRITITADTFPKLFRVYSNFLRGKLYTGACRTGD 192
```

```

; NUMBER OF SEQ ID NOS: 28
; SOFTWARE: PatentIn version 3.2
; SEQ ID NO 22
; LENGTH: 435
; TYPE: PRT
; ORGANISM: Artificial Sequence
; FEATURE:
; OTHER INFORMATION: HuEPO-L-vfc gammal with a 27-amino acid leader peptide (figure
; OTHER INFORMATION: 2C)
US-11-016-518A-22

```

Query Match	Score	DB	Length
Best Local Similarity	100.0%	846;	20;
Matches 165; Conservative	0;	Pred. No. 5.3e-85;	
Mismatches	0;	Indels	0;
Gaps	0;		

Qy	1	APPRLLCDSRVLRVLLRAKEAENITTGCAEHCSSLNENITVPDTKVNFVANKMEVGGQA	60
Db	28	APPRLLCDSRVLRVLLRAKEAENITTGCAEHCSSLNENITVPDTKVNFVANKMEVGGQA	87
Qy	61	VEVWQGLALLSEAVLRGQALLNSSQPWEPLQLHVDKAVSGLSRLTTLRALGAQKEAIS	120
Db	88	VEVWQGLALLSEAVLRGQALLNSSQPWEPLQLHVDKAVSGLSRLTTLRALGAQKEAIS	147
Qy	121	PPDAASAAPLRTITADTFRKLFRVYSNFIIRGKLLKLTGCACTGD	165
Db	148	PPDAASAAPLRTITADTFRKLFRVYSNFIIRGKLLKLTGCACTGD	192

```

RESULT 63
US-11-017-185-22
; Sequence 22, Application US/11017185
; Publication No. US20050142642A1
; GENERAL INFORMATION:
; APPLICANT: Sun, Lee-Hwei K
; APPLICANT: Sun, Bill N
; APPLICANT: Sun, Cecily R
; TITLE OF INVENTION: Fc fusion proteins of human erythropoietin with increased biological activity
; TITLE OF INVENTION: activities
; FILE REFERENCE: 02SUN2001D2
; CURRENT APPLICATION NUMBER: US/11/017,185
; CURRENT FILING DATE: 2004-12-17
; PRIOR APPLICATION NUMBER: US 09/932,812
; PRIOR FILING DATE: 2001-08-17
; NUMBER OF SEQ ID NOS: 28
; SOFTWARE: PatentIn version 3.1
; SEQ ID NO 22
; LENGTH: 435
; TYPE: PRT
; ORGANISM: Artificial Sequence
; FEATURE:
; OTHER INFORMATION: HuEPO-L-vFc gammal with a 27-amino acid leader peptide (Figure 2C)
; OTHER INFORMATION: )
US-11-017-185-22

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Query Match	100.0%	Score	846;	DB	20;	Length	435;
Best Local Similarity	100.0%	Pred. No.	5.3e-85;				
Matches	165;	Conservative	0;	Mismatches	0;	Indels	0;
						Gaps	0;

[illegible]

RESULT 64
US-09-932-812-18

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; Sequence 18. Application US/09932812
; Publication No. US20030082749A1
; GENERAL INFORMATION:
; APPLICANT: Sun, Lee-Hwei K
; APPLICANT: Sun, Bill N
; APPLICANT: Sun, Cecily R
; TITLE OF INVENTION: FC fusion proteins of human erythropoietin with increased biolo
; FILE REFERENCE: 02SUN2001
; CURRENT APPLICATION NUMBER: US/09/932,812
; CURRENT FILING DATE: 2001-10-30
; NUMBER OF SEQ ID NOS: 22
; SOFTWARE: PatentIn version 3.1
; SEQ ID NO 18
; LENGTH: 436
; TYPE: PRT
; ORGANISM: Artificial Sequence
; FEATURE:
; OTHER INFORMATION: HuEPO-L-vFc gamma2 with a 27-amino acid leader peptide (Figure
; US-09-932-812-18
; OTHER INFORMATION: A)
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	Query Match	100.0%;	Score 846;	DB 10;	Length 436;
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Qy	1	APPLICDSVLYRYLLEAKEAENITTCGAHCSLNENITVPDTKVPFYAWKRMVEVGOQA	60		
Db	28	APPLICDSVLYRYLLEAKEAENITTCGAHCSLNENITVPDTKVPFYAWKRMVEVGOQA	87		
Qy	61	VEVWQGLALSEAVLRQALLVNSQWPPEQLQHVDKAVSGRLSLTLLRALGAKQKEAIS	120		
Db	88	VEVWQGLALSEAVLRQALLVNSQWPPEQLQHVDKAVSGRLSLTLLRALGAKQKEAIS	147		
Qy	121	PPDAASAAPLRTITADTFRKLFRVYSNFLRGKLYTGEACRTGD	165		
Db	148	PPDAASAAPLRTITADTFRKLFRVYSNFLRGKLYTGEACRTGD	192		

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RESULT 65
US-10-761-593A-18
; Sequence 18, Application US/10761593A
; Publication No. US20040175824A1
; GENERAL INFORMATION:
; APPLICANT: Sun, Lee-Hwei K
; APPLICANT: Sun, Bill N
; APPLICANT: Sun, Cecily R
; TITLE OF INVENTION: Fc fusion proteins of human erythropoietin with high biological
; TITLE OF INVENTION: activities
; FILE REFERENCE: 02SUN2001-A
; CURRENT APPLICATION NUMBER: US/10/761,593A
; CURRENT FILING DATE: 2004-01-21
; PRIOR APPLICATION NUMBER: 09/932812
; PRIOR FILING DATE: 2001-08-17
; NUMBER OF SEQ ID NOS: 28
; SOFTWARE: Patentin version 3.2
; SEQ ID NO 18
; LENGTH: 436
; TYPE: PRT
; ORGANISM: Artificial Sequence
; FEATURE:
; OTHER INFORMATION: HuSP0-L-vFc gamma2 with a 27-amino acid leader peptide (Figure
; OTHER INFORMATION: 2A)
US-10-761-593A-18

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Query Match	100.0%	Score 846	DB 16	Length 436
Best Local Similarity	100.0%	Pred. No. 5.3e-85		
Matches 165	Conservative 0	Mismatches 0	Indels 0	Gaps 0
Qy 1	APPLICDSRVLYRLLEAKEAENITTCGCAEHCSLNENITVPDTKVFYAWKMEVGOQA	60		
Db 28	APPLICDSRVLYRLLEAKEAENITTCGCAEHCSLNENITVPDTKVFYAWKMEVGOQA	87		
Qy 61	VEVVOGLALISVAVLRCQALLVNSQSPWEPLQLHVDKAVSGLSRLTLLRALGAQKAIS	120		

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; CURRENT FILING DATE: 2004-01-21
; PRIOR APPLICATION NUMBER: 09/932812
; PRIOR FILING DATE: 2001-08-17
; NUMBER OF SEQ ID NOS: 28
; SOFTWARE: PatentIn version 3.2
; SEQ ID NO 20
; LENGTH: 437
; TYPE: PRT
; ORGANISM: Artificial Sequence
; FEATURE:
; OTHER INFORMATION: HUEPO-L-vfc gamm
; OTHER INFORMATION: 2B)
US-10-761-593A-20

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[illegible]

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RESULT 70
US-11-016-518A-20
/ Sequence 20, Application US/11016518A
/ Publication No. US20050124045A1
/ GENERAL INFORMATION:
/ APPLICANT: Sun, Lee-Hwei K
/ APPLICANT: Sun, Bill N
/ APPLICANT: Sun, Cecily R
/ TITLE OF INVENTION: Fc fusion protein
/ TITLE OF INVENTION: biological activ
/ FILE REFERENCE: 02SUN2004D1
/ CURRENT APPLICATION NUMBER: US/11/016518A
/ CURRENT FILING DATE: 2004-12-17
/ PRIOR APPLICATION NUMBER: US 09/932,812
/ PRIOR FILING DATE: 2001-08-17
/ NUMBER OF SEQ ID NOS: 28
/ SOFTWARE: PatentIn version 3.2
/ SEQ ID NO 20
/ LENGTH: 437
/ TYPE: PRT
/ ORGANISM: Artificial Sequence
/ FEATURE:
/ OTHER INFORMATION: HuEP0-L-vFc gamma
/ OTHER INFORMATION: 2B)
US-11-016-518A-20

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	Query Match	100.0%	Score 846;	DB 20;	Length 437;
	Best Local Similarity	100.0%;	Pred. No. 5.3e-85;		
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Qy	1	APRLICDSVLYRLLYLEAKEAEENITTCGAHCSLNENITVPDTKUNFYAKWMEVQQA	60		
Db	28	APRLICDSVLYRLLYLEAKEAEENITTCGAHCSLNENITVPDTKUNFYAKWMEVQQA	87		
Qy	61	VEVWQGLALISEAVLRQALLVNSSQPWEPLQLHVDKAVSGLSRLTLLRALGAKQEAIS	120		
Db	88	VEVWQGLALISEAVLRQALLVNSSQPWEPLQLHVDKAVSGLSRLTLLRALGAKQEAIS	147		
Qy	121	PPDAASAAPRTTADTFRKLFRVYSNFLRGKLLKLTGEACRTGD	165		
Db	148	PPDAASAAPRTTADTFRKLFRVYSNFLRGKLLKLTGEACRTGD	192		

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RESULT 71
US-11-017-185-20
; Sequence 20, Application US/11017185
; Publication No. US20050142642A1
; GENERAL INFORMATION:
; APPLICANT: Sun, Lee-Hwei K
; APPLICANT: Sun, Bill N
; APPLICANT: Sun, Cecil R
; TITLE OF INVENTION: FC function proteins of
; TITLE OF INVENTION: activities
; FILE REFERENCE: 02SUN2001D2
; CURRENT APPLICATION NUMBER: US/11/017,185
; CURRENT FILING DATE: 2004-12-17
; PRIOR APPLICATION NUMBER: US 09/932,812
; PRIOR FILING DATE: 2001-08-17
; NUMBER OF SEQ ID NOS: 28
; SOFTWARE: PatentIn version 3.1
; SEQ ID NO 20
; LENGTH: 437
; TYPE: PRT
; ORGANISM: Artificial Sequence
; FEATURE:
; OTHER INFORMATION: HuEPO-L-vFc gamma4 w/
; OTHER INFORMATION: )
US-11-017-185-20

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	Query Match	100.0%	Score 846;	DB 20;	Length 437;
	Best Local Similarity	100.0%;	Pred. No. 5.3e-85;		
	Matches 165;	Conservative 0;	Mismatches 0;	Indels 0;	Gaps 0;
Qy	1	APPRLICDSVRLERYLLEAKAEENITTCGCAEHCSLNENITVPDTKKNFYAWKRMVEVQQA	60		
Db	28	APPRLICDSVRLERYLLEAKAEENITTCGCAEHCSLNENITVPDTKKNFYAWKRMVEVQQA	87		
Qy	61	VEVWQGLALLSEAVLRGQALLVNSSQWPPEQLQHFVDKAVSGLSRLSTLLLRALGAQKEAIS	120		
Db	88	VEVWQGLALLSEAVLRGQALLVNSSQWPPEQLQHFVDKAVSGLSRLSTLLLRALGAQKEAIS	147		
Qy	121	PPDAAGAAPLRTTTADTFRKLFRVYNFNLRGKKLYTGEACRTGD	165		
Db	148	PPDAAGAAPLRTTTADTFRKLFRVYNFNLRGKKLYTGEACRTGD	192		

Search completed: August 23, 2005, 14:18:57
Job time : 67 secs